TuftScope

The Interdisciplinary Journal of Health, Ethics, and Policy

April 2004 Volume 4

Original Articles

A Publication of TuftScope,
A Student Organization at Tufts University

TuftScope

The Interdisciplinary Journal of Health, Ethics, & Policy

TuftScope
Mayer Campus Center
Tufts University
Medford, MA 02155

ISSN 1534-7397

TuftScope is published by Turley Publications
Palmer, MA

With recent advances in biotechnology and advanced medical techniques comes a multitude of ethical and philosophical questions, and a need for policy review. Conceived in the Fall of 2000 by undergraduate students, *TuftScope: The Interdisciplinary Journal of Health, Ethics, & Policy* brings together various students, academics, policymakers, and industry representatives to talk about pertinent healthcare and biosocial debates in today's world.

TuftScope accepts original articles on governmental health policy, public health, bioethics matters, medical education, research in the mentioned fields, and other various issues dealing with the science and art of medicine or our country's healthcare system. The principle objective of TuftScope is to bring together seemingly different perspectives, citizenship and the health sciences, to transform thoughts and ideas into active citizenship and working policies.

TuftScope is a recognized, funded student organization of Tufts University.

Electronic Access
http://www.tuftscope.org

General Inquiries
info@tuftscope.org

Advertising Information
www.tuftscope.org
business@tuftscope.org

TuftScope
The Interdisciplinary Journal of Health, Ethics, and Policy
April 2004 Volume 4

Original Articles

Correspondence

In The News

On the Web

Get Full Text Articles
Participate in Discussion Forums
Visit TuftScope Conference Websites
Read Guidelines for Authors
Request Reprints

www.tuftscope.org

TuftScope
The Interdisciplinary Journal of Health, Ethics, and Policy
April 2004 Volume 4

HORMONE REPLACEMENT THERAPY: THE END OF THE FOUNTAIN OF YOUTH

Kate Gluckman

In May 2001 the Women's Health Initiative (WHI), a study funded by the National Heart, Lung, and Blood Institute to determine the long term effects of hormone replacement therapy (HRT), was stopped after a dangerous increase in invasive breast cancer was seen among women taking the supplementary estrogen/progestin pill. Researchers also reported an increase in coronary heart disease and strokes among the women receiving HRT. A decrease was seen in the incidence of colorectal cancer and hip fracture, supporting previous research that estrogen may have a preventative effect on osteoporosis in aging females. Absolute excess risks per 10,000 people per year were also evaluated and found that HRT contributed seven more coronary heart disease events, eight more strokes, and eight more incidents of breast cancer compared to untreated women. The first study of its kind, WHI offered a complete view of the effects of long term HRT use on multiple diseases and the aging process in women. This paper compares and contrasts hormone replacement therapy before and after the Women's Health Initiative, as well as investigates the media and social attitudes about menopause and HRT throughout the last fifty years. Through this discussion a parallel can be drawn between the lack of long term research on HRT and the male-centered marketing strategies that have supported a negative social attitude towards menopause. Although it is impossible to conclude a causal effect between these two variables, this paper touches on the powerful influence of public media and attitude on scientific thought and progress.

In the summer of 2002 the magical fountain of youth dried up. For the first time in the history of Hormone Replacement Therapy (HRT), a study by the Women's Health Initiative (WHI) stated that long-term use of HRT increased the risk of heart disease, breast cancer, and blood clots in healthy menopausal women. After sixty years of popular success, HRT has been stripped of its promise of immortality and many concerns are now being raised about the safety of this drug therapy. The research community and pharmaceutical companies are also being criticized for the thirty-year period where HRT was on the market without scientific backing to support its sales. Two factors may have played into the lack of knowledge about HRT and the delay in conclusive data: the lack of long term research on the drugs, and an inherently sexist and negative aura surrounding menopause and aging women. The following discussion examines the connection between the social and scientific aspects of HRT. It also analyzes why -- after so many years of blind faith -- long-term studies of the effects of hormone replacement are being funded, and a public shift in attitude is taking place.

History of HRT

The fountain of youth has mystified and motivated many throughout history. From the days of Ponce De Leon, the possibility of eternal life has fueled the fire of exploration and discovery. The elusive liquid of the fountain promises to return all that everyday life steals: energy, radiance, and beauty. Women, especially, desire everlasting youth, and their obsession is fueled by magazines, movies and constant pressure from the opposite sex. In the United States the pressure is particularly high as society devalues the aging and elderly, citing their cost to society and their uselessness. There has been a constant search for the fountain of youth in the era of medical advances and increased health awareness. For the population of women going through menopause this search has

been particularly frantic and has centered on the primary female sex hormone estrogen.

In 1942 the estrogen replacement pill Premarin was put on the market. This drug was created from the urine of pregnant mares, and promised to alleviate acute symptoms of menopause including hot flashes, mood swings, vaginal dryness, and insomnia[1]. Drug companies continued with these promises for decades as more and more women bought into this medical youth remedy. By 1970, over thirty million prescriptions for HRT were handed out in the United States alone. HRT not only promised temporary relief from menopause, but also the possibility of protection against long term diseases such as breast cancer, heart disease, dementia and osteoporosis. To menopausal women estrogen was the answer. To the drug companies, menopausal women were a huge market.

History of Research on HRT

To the scientist, estrogen was still somewhat of a mystery. As of 1970, research on estrogen replacement therapy focused on the short-term use of the drug, and had shown great success. During the summer of 1960, *The New England Journal of Medicine* recommended hormone replacement therapy for "everyone with evidence of an estrogen lack"[2]. However, long term research had yet to be conducted even though the hormone replacement pill was becoming one of the most widely distributed drugs in the country[3]. Drug companies not only wooed women to the drug, but also appeared to have enlisted the help of the scientific community in their marketing campaign.

It was not until December 4, 1975 that D.C. Smith, et al., published results in the *The New England Journal of Medicine* showing that estrogen replacement hormone therapy increased the risk of uterine cancer, specifically endometrial carcinoma[4]. It was concurrently discovered that offering a progestin additive to the estrogen inhibited these negative effects. Women with hysterectomies continued with the estrogen therapy, while healthy women were given the combination hormone replacement drug[5]. More research occurred in 1987 with the Postmenopausal Estrogen/Progestin Interventions Trials (PEPI), which tested the effectiveness of four varying ratios of estrogen and progestin on the reduction of LDL cholesterol and the decrease of blood clots in menopausal women. Results found significant decreases in LDL and blood clotting for all ratios. Although these results supported HRT as a method of long-term health care, the study population was limited to 875 mostly white women and only lasted three years, creating very little external validity to the general public. The research was limited to cholesterol assays and did not address the more pressing issues of breast cancer and heart disease[6]. Thus, it was impossible to distinguish through Smith's research whether HRT had a positive effect of women's long-term health, or whether healthy women were just more likely to be included in this kind of study. Two years later, *The New England Journal of Medicine* reported that women on HRT had increased risk of breast cancer compared with a placebo group. L. Berjkvist, et al., compared estrogen replacement therapy to the drug combination of estrogen and progestin and found that women on the combination treatment had a higher incidence of cancer than the placebo and estrogen groups[7]. Then over a half-century-old, the benefits and problems of long term HRT were still largely unknown and contradictory. Despite the preliminary findings suggesting that HRT could have positive effects on short term menopause relief, one must question how the FDA and other regulatory boards allowed the approval of HRT without conclusive and thorough research on the effects of long term use. The social stigmas attached to menopause and the need to medicate menopausal women may have influenced regulators decisions on HRT, as could the financial and political pressure from drug manufacturers producing hormone replacement pills.

History of Menopause Marketing

The history of women's health issues in the United States has been one of inherent sexism and ignorance. The medical professions in the 1940's and 50's were male dominated and scientific thought was highly saturated with social stigmas. Women were viewed as reproduction vehicles. The presence of active ovaries and estrogen within a women's body elevated her status in society. Once

those processes naturally ceased, the woman was devalued. This philosophy created a negative representation of menopause and aging in general for women. These negative attributes attached with aging are present all over the world, yet seem to be emphasized in the United States. As a culture we do not respect our elders, but rather view them as a drain on social resources. In response to this social consciousness, Americans express more symptoms of menopause than women in other countries. For instance, women in Asia report symptoms on lower levels and Mayan women in Mexico do not complain of hot flashes at all[3]. It appears that menopause is labeled a disease because it has been depicted as one.

Marketing strategies in the past have used sexist commentary to increase the apparent necessity for hormone replacement therapy. Within our patriarchal society, we see public texts not only address the effects of menopause on women, but also the effects on the men that live with them. Arnold Lorand's *Old Age Deferred* is a perfect example. He states "not only for the wife, who is directly affected by it, but also in almost equal degree for the husband, who must show the greatest forbearance"[2]. During the 1970's, drug companies created supposed educational films for doctors to learn more about HRT. One such movie explained the mental state of menopausal women and her fears for old age, "When a woman develops hot flashes, sweats, wrinkles on her face, she is quite concerned that she is losing her youth – that she may indeed be losing her husband"[1]. In ads menopause was never portrayed as a natural process in the lives of all women, rather it was an illness that effected health, beauty, and sexuality, and therefore had a negative impact on the lives of males. HRT became popular in women not only to help with the symptoms of menopause, but also to please and satisfy their male counterparts. In terms of effectiveness for drug companies, targeting the male population was an intelligent move, since for the majority of the 1900's it was the males that worked outside the home, providing their wives with financial support. Male-targeted advertising focused on the population with financial assets. It may have outlined the benefits of HRT for females, but was careful to describe the indirect benefits males could gain by supplying their wives with medication. These ads characterized menopause as an abnormal state in dire need of correction by the medical community.

Feminine Forever, a book written by Dr. Robert Wilson in 1966 perpetuated the negative stigmas of menopause and created a fury of HRT prescription. Wilson, a physician, was hired by three pharmaceutical giants, Searle, Upjohn, and Wyeth-Ayerst to write *Feminine Forever* and thereby create the perception that HRT was necessary for all women, not just those suffering from disabling menopausal symptoms. In following with previous marketing techniques, Wilson targeted menopause's effects on the husband. He gave anecdotal stories about how rampant husbands would come into his office and offer all amounts of money so to have him save their wives from menopause and old age. If their wives continued to act as they were, the husbands swore they would murder them[8]. Wilson writes,

Outright murder may be a relatively rare consequence of menopause - though not as rare as most of us might suppose. Yet the psychological equivalent of murder in the form of broken family relations and hatred between husband and wife is a common result of menopausal change. Medical statistics can never convey the staggering total of sheer misery inflicted upon such families by menopausal side effects.

As we can see through marketing techniques and social commentary, much of the past coverage of menopause and HRT has been based on sexist beliefs rather than biological explanations.

Modern Phase of HRT Research

It wasn't until the 1990's that the medical community finally took initiative and began researching the effects of HRT using high quality scientific techniques. The Wyeth-Ayerst Drug Manufacturing Company funded the first substantial study after the FDA rejected their application for approving HRT as a treatment for cardiovascular disease[9]. The Heart and Estrogen-Progestrin Replacement Study (HERS) began in 1993 and followed women with a history of heart disease for approximately four years. The hypothesis of HERS was that HRT

would help prevent a second incident of coronary disease. The initial results were negative, researchers saw a increase of coronary heart disease in the first year of the study, and no overall benefit after 4.2 years[9]. HERS also found an increase in breast cancer, heart attacks, and blood clots in the legs and lungs[6]. The first study of its kind, HERS set the standard for future research with its randomized, controlled, and double blind design. Researchers included other risks of coronary heart disease including obesity, smoking, and exercise levels. There was a complete evaluation of the women's lives to understand the effects of HRT on heart disease. Critics of the study stated that the population sample of women with coronary heart disease limited the ability to generalize the results, as did the racial homogeneity of the women. HERS results did not disclose how HRT affects healthy women nor did it address the long-term effects of the therapy.

A second study continued monitoring these women for approximately two years longer to assess the longer term effects of HRT on coronary heart incidents. HERS II had a 93% surviving rate from HERS and continued with the estrogen/progestin therapy. Results indicated that HRT did not reduce the risk of heart disease and should not be used as medication to do so[10]. This study offered some insight into long-term therapy on women with heart disease, and was at that time the longest HRT study completed. As with the HERS, however, the results were not applicable to entire populations of menopausal women.

The most recent study was funded by the National Heart, Lung, and Blood Institute (NHLBI), after Congresswomen Pat Schroeder and other female legislators argued for more comprehensive studies on women and aging. Beginning in 1997, the Women's Health Initiative recruited healthy menopausal women, and developed a comprehensive study to look at the long-term effects of HRT on dependent variables including coronary heart disease, invasive breast cancer, stroke, colorectal caner, hip fracture, and pulmonary embolism. With a controlled, randomized, and double blind design, researchers correlated HRT with a variety of health outcomes. WHI used Prempro, the most popular HRT drug as their estrogen/progestin pill. 16,608 women between the ages of 50 and 79 participated in the research[11].

On May 31, 2001 an independent board of overseers decided that the increase of invasive breast cancer seen among the women taking the estrogen/progestin pill was above the critical level and the study should be stopped before the adverse effects became greater. Researchers also found an increase in coronary heart disease and strokes. A decrease was seen in the incidence of colorectal cancer and hip fracture, supporting previous research stating that estrogen may help prevent osteoporosis. Absolute excess risks per 10,000 people per year were also evaluated and found that HRT contributed seven more coronary heart disease events, eight more strokes and eight more incidences of breast cancer[11]. Concerns were raised about the applicability of the Prempro study to other HRT pills on the market, which offer varying ratios of estrogen and progestin and might produce different results[2]. WHI head researcher Dr. Jacques Rossouw agreed with such concerns, and also reminded the public not to generalize the results to short term use of HRT, which still appeared to have positive benefits[12]. The results of WHI have changed the outlook on HRT and Prempro. Wyeth Pharmaceuticals, in particular, noticed the effects immediately, as their stock dropped twenty-five percent during the summer of 2001.

An interesting effect of the WHI study results is that current studies of HRT are having trouble maintaining their population size. The Women's International Study of Long Duration Oestrogen after Menopause (WISDOM) was due to end in 2012, yet concluded in November of 2002 as their participants dwindled. This effect is understandable yet unfortunate due to the excellent study population organized for WISDOM. Participants were women from the UK, Australia, and New Zealand and represented a greater diversity than populations in previous studies. The WHI results were excellent and highly valid on long-term use of HRT, but much more research is needed to verify the results and look at other menopausal and aging issues. The lack of willing participants in future HRT studies, and the premature termination of

WISDOM is devastating for this still relatively new field of study.

The WHI results may have hampered human studies of long-term use of HRT, but they appear to have had an opposite effect on animal studies. An article in the November 14, 2003 issue of *Science* addresses the inconsistencies between animal research on estrogen replacement and human trials. Much research has been done using rats and estrogen therapy, and the majority of the results state that the drug is correlated with an increase in cardiovascular health. These results contradict the results of WHI study and other human studies. Researchers, including Dr. Michael Mendelsohn of the Tufts-New England Medical Center, criticize WHI for not replicating exactly what has been tested in animals. Mendelsohn contends that the women in the study were older than most menopausal women, and that the dose of Prempo was too high. He believes that the application of the drug may have changed the way that the estrogen was metabolized. The drug is given subcutaneously to animals in the lab, while women in the study took the pill orally. Mendelsohn also suggests that the addition of progestin may be leading to a decreased effectiveness of the estrogen on cardiovascular health, and that there are very few animal studies that have used combination hormone therapy[12]. After the results of the WHI were published scientists began to organize studies in an effort to decrease the disparities between the animal and human testing. The future of HRT testing will rely on the results obtained from animal laboratories, and will most certainly shape the direction this field of study will take.

HRT in the Current Media and Society

As the research on HRT changed, so did public coverage of menopause and hormone therapy. A general shift from the sexist social agenda created opportunities for varied views in the scientific and social realm. The drug companies still controlled much of the information about HRT, but there was a shift from focusing on menopause as it affected the male population to labeling menopause as a change in the female body. This turn in emphasis is more logical and fair to women, yet it still insinuates that menopause is a disease, and that it leaves the woman in a deficient state. Drug companies use the image of menopause as a disease to push their drugs upon the female population. Using celebrities such as Patti Labelle[9], HRT has become the drug of choice, not to satisfy the man, but to satisfy a women's body. As in the 1950's, women still fear growing older and the increased risk of age related disease such as osteoporosis. Drug companies continue to play on this trepidation. The pharmaceutical giant Merck recently ran an ad portraying a woman cowering under the looming cloud of osteoporosis and the threat of depending on a wheelchair[3]. As in many drug commercials, the product being sold is not mentioned, nor its purpose.

Alternatives to drugs have also become popular in the modern marketing of menopause. Soy products, including milk, shakes, energy bars, and nuts have been very successful. The National Institute of Health is currently studying the therapeutic effects of herbs, such as black cohosh and red clover, on menopausal symptoms. Preliminary results have found no side effects, and women seem to be pleased with the benefits. Lifestyle changes, however, are hardly mentioned as a method to prevent many diseases associated with aging. The cessation of smoking and daily exercise can aid with osteoporosis and heart disease. Exercise can also help with the mood swings associated with the acute symptoms of menopause[9].

Tufts University, in cooperation with Dr. Miriam Nelson at the Gerald J. and Dorothy R. Friedman School of Nutrition, Science, and Policy, has developed and organized a program to address such issues. Dr. Nelson is the author of the *Strong Women* book series, a collection of books that educate women on healthy eating, exercise, and lifestyle modifications. The *Strong Women* program, run by the Tufts University Personalized Performance Program, takes the scientific information from Nelson's work and applies it to a weight lifting class for older women. The class meets twice a week and lasts one hour. The women participate in multiple exercises aimed at reducing the risk of osteoporosis, which increases at the age of menopause. Nelson's research on osteoporosis

indicates that load bearing exercise slows the process of bone loss and may prevent osteoporosis in some women[13]. The *Strong Women* program is currently in its second year and has received wide praise from the Tufts community.

An increase in education and marketing can be seen in products directly targeted towards women including health magazines and women related television shows. On October 2, 2002 the *Oprah Winfrey Show* ran a segment entitled "Mammograms, Self-exams, Hormone Therapy - Why are we so confused?" Presenting the results of WHI, Ms. Winfrey and two female doctors discussed the state of menopause and HRT research today. Dr. Judith Reichman reminded the audience that the recent WHI results were specific to Prempro, and that the short-term benefits were still extant for HRT. Dr. Susan Love, author of *Dr. Susan Love's Breast Book*, discussed the misconception of menopause as a disease that needs treatment. She indicated that women's bodies going through menopause are designed not to have estrogen and progesterone present, continuous pills are both unnatural and harmful. Oprah Winfrey is one of the most visible and well-known women in the United States. Her discussion of menopause and HRT reached millions of women across the country and represented the coming of age of the topic's discussion. No longer is HRT only spoken about in commercials and science journals, but successful women are speaking out on this subject. Their open discourse on the issues could serve to dispel the negative connotation of menopause and reclaim the aging process as a natural one for women everywhere.

Popular magazines not specializing in women's issues have also taken sides on the topic of HRT. *Time* covered the release of the WHI results with a cover story on July 22, 2002 entitled "The Truth About Hormones". Many of the stereotypes and myths about HRT as the fountain of youth were addressed in the article, as was the history of the research. The authors hypothesize that the positive effects found in early HRT research were due to the healthy lifestyles of women in the sample population. They propose that these lifestyles, and not the administered hormones, were responsible for the decrease in rates of heart disease and breast cancer. The WHI study also used healthy women, and therefore the generalized results exclude women who are already at risk for disease. The article also warns against generalizing the effects found with Prempro to all hormone therapies, and also generalizing to short-term effect. Much research has been done on short-term effects of HRT as we have seen in the early studies, and no negative risks have been found. There was a conscious effort in the *Time* article to not overestimate the effect of the WHI study on the status of HRT in this country. The authors suggest individual medical consultations and emphasize the importance of the personal decision about HRT. The article reports the results of the study directly, without condescension, enabling the reader to determine her own stance on menopause and hormone replacement therapy.

Conclusion

The results of the WHI study changed the face of HRT forever. After the study showed that estrogen and progestin taken for long periods of time increased the chance of heart disease and breast cancer in menopausal women, social naiveté about hormone therapy has begun to disappear. The history of research on HRT's effects on menopausal symptoms has come under scrutiny in the wake of the WHI study. The scientific community and regulatory boards have been forced to examine how almost sixty years of hormone therapy occurred without conclusive research to support its use. When reviewing the past studies, one cannot alienate science from social context. In the past, menopause in the United States has been defined as a women's disease afflicting not only herself but her husband and family. Often menopause has been labeled the "defeminizing" of a woman as she loses her ability to reproduce and declines in beauty and sexuality[8]. Even today, menopause is highly marketed as a disease that is in need of a cure and a drug prescription, rather than a natural process that occurs to all women as they age. Women are constantly bombarded with ads for soy shakes, herbal remedies, and of course HRT.

Post-WHI research will certainly be focused on returning to animal testing for further analysis of estrogen and progestin. Future human based studies

should take the lead from the organizers of WISDOM and create ethnically diverse study populations, as well as researching women of different age groups, such as those who enter menopause in their late forties compared with those in their sixties. The future of HRT and menopause in the media must reflect not only the scientific research being completed, but also the status of women's health in the US. The need for wider coverage of health issues for aging women is certainly apparent, as is the need for highly visible and educated spokeswomen such as Oprah Winfrey and Dr. Miriam Nelson. The continued coverage of and research into HRT and menopause will lead to more knowledge and a greater understanding of the issues involved with women's aging. HRT may not be the elusive fountain of youth that so many women had hoped for, but their dream is not dead, at least not yet.

Author Biography

Kate Gluckman is a senior biopsychology student at Tufts University. *She would like to thank Professor Ross Feldberg for his support and his great enthusiasm towards teaching. She would also like to thank her family, for without them nothing would be possible.*

References

[1] J. Neel. The Marketing of Menopause: Historically, Hormone Therapy Heavy on Promotion, Light on Science. 2002. http://www.npr.org/news/specials/hrt/index.html accessed November 17, 2003.
Neel offers a critique of past HRT research and marketing.

[2] Cowley, G. and Springen K. The End of the Age of Estrogen: Women were told for decades that hormone-replacement therapy would protect their hearts and reserve their youth. Now the evidence is in, and an era is over. Newsweek. July 22, 2002: 38.

[3] P. Babich, R. Gold. Making Contact: Marketing Menopause. 1999. http://www.radioproject.org/archive/1999/9908.html accessed November 19, 2003.
Babich and Gold offer dialog with multiple doctors and to address the past marketing of menopause and how social views have impacted the research. There are feminist undertones to the commentary.

[4] Smith, D.C., Prentic R., Thompson D.J., Herrmann, W.L. (1975) "Association of estrogen and endometrial carcinoma" New England Journal of Medicine **293** (23): 1164-1167.

[5] Gorman, K. and Park, A. The Truth About Hormones: A large federally funded study provides definitive proof that estrogen and progestin are not age-defying wonder drugs. What's a woman to do? Time. July 22, 2002: 32.

[6] The National Heart, Lung, and Blood Institute at the National Health Institute (NHI). Facts about Postmenopausal Hormone Therapy: Information for the public. 2002. http://www.nhlbi.nih.gov/health/women/pht_facts.htm accessed November 11, 2003.
This site covers basic information including results of studies, alternatives to HRT, pros and cons of HRT. Information is directed towards menopausal women.

[7] Bergkvist L., Adami H. O., Persson I., Hoover R., Schairer C. (1989) "The risk of breast cancer after estrogen and estrogen-progestin replacement." New England Journal of Medicine **321**: 293-297.

[8] Feminine Forever. Wilson, R. M. Evans and Co., pub. New York (1966)

[9] Enserink, M. (2002) "The vanishing promises of hormone replacement" Science **297**: 325-326.

[10] Grady, D., et.al. (2002) "Cardiovascular disease outcomes during 6.8 years of hormone therapy: heart and estrogen/progestin replacement study follow-up (HERS II)" Journal of the American Medical Association **288** (9): 49.

[11] Women's Heath Initiative (WHI). (2002) "Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial." Journal of the American Medical Association **288** (13): 321.

[12] Couzin, J. (2003) "Estrogen research: the great estrogen conundrum" Science **302**: 1136-1138.

[13] Nelson, Miriam Elizabeth. Bone Health in Young and Old Women: Consequences of Physical Exercise, Hormone Status, and Diet. Boston, MA: Tufts University (1987)

TuftScope
The Interdisciplinary Journal of Health, Ethics, and Policy
April 2004 Volume 4

The Promise of the Human Genome Project: Pharmacogenetics and Race-Based Categorization

Hilary Glazer

The Human Genome Project has promised us much, but to what extent has it fulfilled these promises? This article examines the theoretical utility, practicality, and ethics of pharmacogenetics. Pharmacogenetics is the study of genetic factors that influence a person's response to a drug, specifically with respect to maximizing efficacy and minimizing toxicity. Though it is a potentially beneficial use of the data supplied by the Human Genome Project, pharmacogenetics in its practical application is more debatable—mainly due to the problem of determining individual genotypes. The genetic diversity within the human population is vast. Pharmacogeneticists have suggested that the human population be divided into genetically similar clusters in order to assist in the isolation and prediction of genetically programmed differences in drug responses. However, the suggested means by which to create these clusters have sparked much controversy. Many pharmacogeneticists believe that race is best genetic indicator, and advocate the development and prescription of race-specific drugs. The extent to which race-based pharmacogenetics may benefit or harm society is discussed in this paper. Differing interpretations of the term "race" are explored, in terms of both the classifications used in popular culture and in scientific research. Common misconceptions in current literature on pharmacogenetics are addressed, and the importance of ancestry in the definition of "race" is emphasized. The usefulness and practicality of race-based classification versus individual genotyping are compared, and current examples of the preliminary incorporation of racial differences into drug development are described. This paper also discusses the negative stigma associated with the use of race as a social categorizing tool, counterbalancing it with the positive health benefits associated with using race as a predicative medical tool. The author determines that race-based classification is scientifically justifiable. She then concludes that it is, at present, the best way in which pharmacogenetics can be incorporated into medicine and data from the Human Genome Project can be utilized to its fullest potential.

In June of 2000, the first draft of the human genome was completed. The largest and most extensively funded national science project since the Apollo space mission[1], the Human Genome Project was expected to transform all aspects of biology and medicine in the twenty-first century. By providing an inventory of every human gene, especially the ones linked to prevalent diseases such as diabetes, cardiovascular disease, and cancer, the Human Genome Project promised to give us a deep understanding of human biology such that customized health care would be possible. To what extent has genetic research actually fulfilled these promises? In an article published in *The New England Journal of Medicine* one month after the initial draft was completed, Neil A. Holtzman and Theresa M. Marteau seriously questioned the biological assumptions underlying many aspects of the Human Genome Project, citing the complexity involved in determining the genetics behind common diseases and science's inability to predict individuals' susceptibility to them[2]. In fact, many skeptics point to sickle-cell anemia, a prevalent disease whose genetic cause has been known for more than 40 years, but for which researchers have failed to find a completely effective treatment[1]. Holtzman and Marteau even claimed that medicine was being shrouded "in a genetic mantle [that] may prove to be like the emperor's new clothes..." In their view, the real culprits of disease, such as differences in social structure, lifestyle and overall environment, were being mistakenly overlooked.

Will genetics truly give rise to customized healthcare, tailored to the 0.1% genetic difference that exists between us?[3] Instead of revealing how genes indicate a predisposition to disease, many have suggested that our knowledge of the human genome may in fact better be used to create individual drug response profiles and tailor both the choice and dosage of drugs to these profiles. Dr. Werner Kalow, for example, claims that the clearly definable chemical nature of drugs—our ability to precisely measure their phenotypic effects and their fate in the body—gives all the more credence to this specific application of genetics to medicine.[4] It has also been suggested that because general practitioners may more easily understand pharmacogenetic information than genetic principles, the integration of genetic medicine into healthcare may be more effectively carried out with respect to drug response rather than susceptibility to disease.[5] Even Holtzman and Marteau in the same July 2000 paper expressed confidence in predicting inherited differences in sensitivity to drugs as compared to genetic predisposition to disease.

Pharmacogenetics has been defined as the study of genetic variability in drug response[5], and many of its proponents claim it will transform medicine from a largely trial-and-error-based process to one of much greater specificity and efficacy. Most pharmaceutical companies currently develop drugs by testing animals and screening humans, using measurements like LD_{50} and ED_{50}, the dose of a drug that killed or had the expected effect in 50% of population, respectively. Moreover, they base the majority of their decisions on such statistical criteria without ever even attempting to define the cause of the often-large variation in dose response[4]. Doctors also treat patients based on a limited scope of statistical criteria, including symptoms, age, and weight[6], as well as so-called *standard doses*, which may have toxic effects in some patients and be ineffective in others. This lack of pharmacological specificity largely centers around the fact that one disease often has several different causes, leading to differences in responsiveness to the same medicine[7] as well as frustration on the part of both patients and physicians, who can only adjust dosages after observing a drug's initial effects[8].

Pharmacogenetics attempts to solve these problems. It considers all elements involved in the binding forces between a drug and the proteins with which it interacts, mainly focusing on inter-individual differences in drug absorption, distribution, metabolism, and excretion[9]. It has been discovered that unusual or exceptional inherited differences in drug-metabolizing capacity are generally monogenic traits[7,10], and pharmacogeneticists have been able to capitalize on the fact that the 0.1% genomic differences represent roughly 3 million base pairs[11], with variation occurring every 500-1000 bases in the entire human genome. Particular attention has been paid to single nucleotide polymorphisms (SNPs), or single base pair mutations closely linked to certain allelic differences in drug metabolism, as a way of creating individual drug response profiles[5]. One of the first and most important clinical observations of inherited differences in drug response was made during a clinical trial in the 1970's. After being administered standard doses of the high blood pressure medication debrisoquine, certain patients experienced rare, "unpleasant and disturbing" side effects later found to be familial. For example, a completely healthy man participating in the trial suddenly collapsed due to a drastic fall in his blood pressure[12]. Not until the 1980's, however, was it discovered that defects within a single gene—the gene encoding for debrisoquine hydroxylase enzyme CYP2D6 in the human liver—were responsible. It is now known that CYP2D6 metabolizes more than 65 drugs, including anti-depressants and commonly used heart medications[4,7,10].

It has been suggested that these inherited differences in drug metabolism can have a greater influence on the efficacy and toxicity of medications than any clinical variables being used today[10]. The most frequently cited example of the effective integration of pharmacogenetics into modern healthcare is Herceptin, a breast-cancer treatment selectively prescribed to patients with high levels of HER2 oncogene expression, the drug's target. Because Herceptin significantly improves the survival of the minority of patients who over express the HER2 gene, selecting patients based on specific genetic criteria leads to a more informed and

individualized medical decision. As Herceptin is ineffective in the two-thirds of patients who don't over express HER2 [9], using traditional "one-size-fits-all" methods of drug development would have shown Herceptin ineffective on average. Thus, traditional methods would have failed to pinpoint the select few whom it significantly benefits, and most likely would have taken it off of the pharmacological map long before it could reach them.

This example illustrates the merits of personalized medicine. Currently, adverse drug reactions kill 100,000 hospital patients a year, while 2.2 million patients experience serious, but non-fatal, reactions[6]. If the physician can more accurately predict each patient's response to a drug in terms of both efficacy and toxicity, unsafe and ineffective medicine can be avoided more frequently. Furthermore, drug testing in smaller subgroups of the population would lead to an increasing range of specialized, "orphan" medicines and dramatically reduce the cost of drug testing by approximately 40% of the $880 million currently spent to develop "blockbuster" medicines, marketed to all patients[13]. In this respect, prediction of genetic receptiveness to medication is an extremely useful application of knowledge generated by the Human Genome Project that would not only benefit patients, but the drug development industry as well.

Pharmacogenetics is useful—but is it practical? For pharmacogenetics to work, individual drug responses must be accurately determined by the identification of all causal factors. In the case of the CYP2D6 gene, single nucleotide changes caused exceptional adverse reactions. However, even in the group of people homozygous for the wild-type allele, there was still a 20-fold variation in rate of debrisoquine metabolism[7]. It has thus become increasingly likely that individual drug response is usually not governed by a single gene, but by many factors—both genetic and environmental. An individualized drug response can only be designed by identifying each one of the causal factors and the quantitative relationship between them. This knowledge is often currently unavailable and can be costly to attain. Few genes influencing drug response have been identified to date[14].

Therefore, the "guesswork" has not totally been taken out of developing and prescribing personalized medicine. The need to place individuals within the context of population subgroups by categorizing them into genetically definable "clusters" with similar drug effects is pressing if pharmacogenetics is ever to work on a large-scale[15]. How should this be done?

Pharmacogeneticists have long pointed to race as the easiest and most effective dose response indicator. Recent studies linking drug effectiveness to racial categorization, however, have generated a firestorm of controversy. Many of its most adamant critics assert that using race is scientifically imprecise because it carries absolutely no biological significance. In two articles published in *The New England Journal of Medicine*, Dr. Robert S. Schwartz stated that race-based pharmacological research "falls into error by attributing a complex physiological or clinical phenomenon to arbitrary aspects of physical appearance"[16], while Dr. Richard S. Cooper stated that "we can expect genomics increasingly to negate the old-fashioned concept that [genetic] differences...are racially distributed." Critics often point out that the ethnic categories researchers often use—based upon the 2000 US Census and the FDA's January 2003 "advice"—have resulted to a large extent from political lobbying[17], which supports Schwartz's initial claim that "race is a social construct, not a scientific classification."

Many pharmacogeneticists, however, insist that race is not just skin-deep, and in fact reflects inherent genetic differences that can effectively be used in pharmacological applications. In response to Schwartz's claims, proponents of using race for biological classification assert that "a decade or more of population genetics research has documented genetic, and therefore biological, differentiation among the races."[14] Even the earliest pharmacogenetic studies have illustrated obvious racial differences in drug metabolism. One 1953 study focused on the adverse neurological side effects associated with the anti-tuberculosis drug izoniaziad and pinpointed it to the inactivity of the izoniazid-metabolizing enzyme, N-acetyltransferase, which resulted in abnormally high physiological drug levels. 8000 population-based

studies of N-acetyltransferase were conducted between 1963 and 1992 [19], and have shown strong racial variation with respect to the slow-acetylator phenotype, which occurs among approximately 54% of Caucasians, while only among 34% of black Americans and 14% of East Asians[20]. This enzyme has become especially important because it is now implicated in many other physiological processes, including the detoxification of carcinogens and the metabolism of common treatments for cardiac disorders, hypertension, rheumatoid arthritis, depression, and breast cancer[19,20]. In fact, all genetic polymorphisms in drug-metabolizing enzymes vary in frequency among populations, some by as many as twelvefold[15].

However, the fact that most drug effects are not determined by single genes, but by the interaction between many genes[7], proves problematic. Although pharmacogeneticists often study haplotypes, or a set of closely linked genes inherited as a unit, polygenic inheritance leads to a more continuous range of dose responses[10]. In addition, most abnormal drug responses are shared between populations. Cooper states that "as few as three to five common haplotypes capture the bulk of segregating variation at any specific locus...and those haplotypes are generally represented in [all] populations," leading him to conclude that "the distribution of polygenic phenotypes does not suggest that race is a useful category."[17]

Pharmacogeneticists overcome these difficulties by what they call the "edge effect." They compare the normal distribution curves of drug response for two populations, the edges of which are usually not overlapping. Although the means may not be statistically significant, attention is paid to the differences between the edges. This represents a difference in the percentage of abnormal responders (toxic or non-responding) between the two populations, an item of "major clinical concern" which may not be revealed by taking population averages. Therefore, pharmacogeneticists are quick to emphasize that evaluating the biological significance of differences in drug response only by comparing population means can be misleading and cause inaccurate conclusions to be drawn[4].

Critics erroneously dismiss race's utility as a biologically relevant tool by citing that it only accounts for a small portion of the 0.1% genetic difference that exists between us, so that there is more genetic variation between individuals of the same population (75%) than between individuals of different populations (10%)[14,18]. Risch, et. al., on the other hand, contend that these figures lead to misunderstandings or misinterpretations that are both "counter-intuitive" and "factually incorrect"[14]. A study performed by Wilson, et. al. succeeded in clustering individuals based on as few as 20 randomly-chosen genetic markers called *microsatellites*, which shows that creating discrete genetic clusters of humans is indeed possible. Even more indicative, however, is the fact that although Wilson et. al. intended to invalidate the use of ethnic categories by creating drug response profiles based on drug-metabolizing enzyme variants, their results were largely consistent with the 2000 US Census ethnic categories[14,15].

If even its biggest critics can't successfully invalidate it, why is there still such ardent opposition to using racial categorization in research and medicine? One of the answers to this question centers on how we define *race.* Cooper states that "the meaning of the word race is defined by its use," and refers to the classifications of "Asian", "Black", "Caucasian", and "Hispanic" as the definitive "racial/ethnic groups in the US"[21]. In another paper, he states that although "some traits, such as skin color, vary in a strikingly systematic pattern,...race, as we currently define it, [does not] provide an effective system for summarizing that variation."[17]. Furthermore, Wilson, et. al. argue that the "commonly used ethnic labels (such as Black, Caucasian, and Asian) are insufficient and inaccurate," proclaiming instead that their resultant genetic clustering "broadly corresponds to four geographical areas: Western Eurasia, Sub-Saharan Africa, China, and New Guinea." They emphasize the fact that 62% of the Ethiopians fell into the Western Eurasian group—and would therefore be inaccurately placed in a "Black" cluster—while Chinese and New Guineans fell into two entirely separate groups—and would therefore be inaccurately lumped into an "Asian" cluster—in order to further their argument[15].

These arguments, however, fall short of relevance to the actual issue. Although it is indeed true that race is commonly used in popular culture to distinguish between superficial aspects of our phenotypes, such as skin color, facial features, and hair[22], it is important to recognize that racial categorizations in research "have never been based on skin pigment, but on indigenous continent of origin."[14] In every one of their papers, Cooper, Schwartz, and Wilson, et. al. assume that race has been defined as separate from geographic origin, failing to realize that recent research on race centers almost entirely upon self-identified ancestry, and not upon any characteristics observed by researchers. Schwartz states, "the different frequencies of certain blood-group alleles...reflect geographic origins, not race."[16] Another critic even goes so far as to say that the US Census has determined commonly used, misrepresentative racial categories, inaccurately quoting them as "American Indian, Asian, black, white, and Hispanic," in order to support his claim that ancestry is not reflected in the term *race*[23].

On the contrary, US census categories have changed drastically over the years, and race has now become synonymous with ancestry—at least in terms of the methodology used by researchers. Indeed, population genetics studies commonly place subjects into five main groups based on the 2000 US Census: black or African American, white, Asian, native Hawaiian or other Pacific Islander, and American Indian or Alaskan native. Though many of these categories coincidentally correlate with socially defined categories, they are much more specific than those cited above. Whether intentionally or not, they emphasize geographic region of origin (and therefore ancestry) over any superficial aspects used in popular culture, especially when coupled with self-identification[20]. Therefore, the need is not to change the way in which pharmacogeneticists classify genetic heterogeneity within the US population, but rather to modify the inaccurate socially defined categories that fail to include ancestry.

Many critics' arguments can be subsequently dismantled once we recognize that race, as it is now commonly used in research, has been completely redefined. Recall Wilson et. al.'s contention that Chinese, New Guinean, and Ethiopian individuals would have been inaccurately categorized. This assertion is irrelevant once we discern the difference between popular categories and scientific categories. If used as test subjects, New Guineans would have been placed under the Pacific Islander and not the Asian category, which is known to be mainly Chinese. Furthermore, Ethiopians are known to have had significant contact with and be more closely related to Middle Eastern groups than other African groups, and many would have been placed in a Caucasian category. Wilson et. al.'s results even support researchers' use of broad—and perhaps seemingly more superficial—categories. For example, they did not find any subgroups that merited their own categorical distinctions within a predominantly "white" cluster, which included Norwegians, Ashkenazi Jews, and Armenians. Wilson et. al. therefore unintentionally justified placing these ancestrally related subgroups into a broad "white" cluster because they found the genetic differences between them to be significantly smaller than the genetic differences between the four major clusters. Neglecting to include American Indian or Alaskan individuals in their study, Wilson et. al.'s four major groups inadvertently coincided with the ancestral categorizations currently being used in research: Caucasian, African, Asian, and Pacific Islander[14,15].

If this methodology can be universally extended into clinical practices, in which physicians make medical decisions based on a patient's family history regardless of their physical appearance, then race will become almost completely associated with ancestry and medical categorization will become much more precise. Even Cooper, Schwartz, and Wilson, et.al. point to ancestry as a biologically relevant tool. For example, Cooper writes, "it has been well established that population of origin does provide useful information about the distribution of a number of genetic conditions," and "continental race matters in public health."[21] Why should a person's ancestry matter so much in pharmacogenetic categorization? Genetics views human population structure as determined by patterns of mating and reproduction, and geography largely

governs these patterns. Physical barriers between populations, such as mountains, deserts, and large bodies of water, have impeded interaction and have led to *endogamous*, or with-in group mating patterns[20]. This has therefore led to the observation that appeared just this year in the *Journal of Molecular Medicine*: that nucleotide diversity occurs "in a manner broadly consistent with a standard population-genetic model of human evolutionary history."[24] Of the 45 known single-nucleotide mutations in the CYP2D6 gene, for example, only one is found everywhere (in Africa, Europe, and Asia), suggesting that this mutation originated before the human race left Africa, while the other 44 originated while human populations were physically separated from each other. CYP2D6 enzyme inactivity is seven times more common in Europeans than it is in Asians and Africans[7].

Some pharmacogeneticists have even attempted to avoid the misconceptions associated with *race* by replacing it with the term *ethnicity*. Xie et. al. state that "the definition of ethnicity…is different from that of race" because it is a "multidimensional classification that encompasses shared origins, social background, culture, and environment."[25] Redefining race in the context of ethnicity is therefore not only useful in dispelling claims about the biological irrelevance of race, but two other common objections to pharmacogenetics: that variation in environment is the true source of differences in drug response, and that using self-reported race for population stratification is inaccurate. Many critics of pharmacogenetics—and even pharmacogeneticists themselves—point to the importance of considering environmental influences in drug response, including "culture-derived" factors, such as dietary habits, socioeconomic status, level of education, and the quality of the support system[17]. In addition, the accuracy of using self-reported race over genotypic identification, the so-called *race-neutral* approach, has been called into question[15]. Self-reported race, however, actually accounts for more of these "culture-derived" factors than the race-neutral approach because the definition of race has been expanded to include common ancestry as well as common cultural aspects, such as religion, language, and tradition. It has also been acknowledged that differences in socioeconomic status and level of education can coincide with racial differences, a factor that goes unnoticed in simple genotypic identification[14,20]. This has been elucidated by A. J. Karter:

> By ignoring self-identified race, or even when stratifying on race specific genetic markers, environmental culprits may be missed due to our inability to disentangle the residual effects of confounding. If…variation [were] due to racially varying cultural practices, then self-identified race would be a better adjuster than genetic markers given that cultural practices would be maintained over time if its members could not identify each other. The use of self-identified race provides the most practical resolutions for problems of confounding…and…stratification[11].

In addition, it is unlikely that genotyping will soon become available to clinicians worldwide—the cost of the technology involved must continue to drop before widespread application becomes possible. In the meantime, ethnicity seems a much more practical method of patient stratification because it is much easier to note family history than to note genotype[23,24].

How would ethnically based pharmacogenetics be integrated into research and medicine? Several recent studies have examined possible solutions to the problem of responsiveness to heart failure drugs among black Americans, for example. Heart failure is more common in the black population than in any other population in the US, and blacks show poorer outcome even when treated—statistics that may have many genetic as well as environmental explanations[26]. One possible explanation is decreased bioactivity of endogenous nitric oxide, which may lower one's response to angiotensin-converting enzyme (ACE) inhibitors, a type of heart failure medication. This decreased response was illustrated by a study conducted by Exner et. al., in which treatment with enalapril, an ACE inhibitor, failed to significantly reduce blood pressure and hospitalization rate of self-identified

blacks even though a positive drug response was associated with self-identified whites. Racial differences were observed even after adjustment for educational level and the presence of financial distress[27].

These results not only give rise to the possibility of tailoring ACE inhibitors such as enalapril specifically to Caucasians, but they also underscore a possible lack of efficacy in drugs currently available to the black population. Certain pharmaceutical companies have jumped at this opportunity in the drug market, and in March 2001, NitroMed, Inc. asked the FDA to consider approving its recently developed, alternative heart medication, BilDil, specifically for use in the black population[28]. NitroMed received an "approvable" letter from the FDA, meaning that the agency preliminarily regarded the medication to be safe and effective but withheld full approval because certain issues had yet to be resolved. Consequently, NitroMed is still awaiting full FDA approval and has initiated race-specific clinical trials[18].

Ethnic differences in drug response may therefore lead researchers as well as physicians toward the ultimate goal of personalized medicine. However, it is important to remember that race is merely a surrogate factor used before all causal factors related to drug response can be identified. It is certainly not the be-all, end-all of pharmacogenetics, and inevitable problems arise if racial differences are viewed this way. Even though a plethora of studies, for example, have illustrated that black populations are much poorer responders to ACE inhibitors than white populations, Craig Venter astutely pointed out in a 2003 issue of Australia's *Pharmacy News* that "this does not mean that all blacks, or even most blacks, should respond poorly to such drugs"[29]. Even Exner et. al., in their study of variation in enalapril response, admit that "racial categorization is only a surrogate marker" and that "any identified differences will certainly not apply to all the members of each stratified group."[27] Consider the N-acetyltransferase studies, in which strong racial differences in drug metabolism were repeatedly demonstrated. Although Caucasians exhibited the highest percentage (54%) of the slow acetylator phenotype as compared to blacks (34%) and East Asians (14%), the clinical use of this data is questionable. Would a physician selectively prescribe a certain heart medication only to blacks and East Asians, just because an adverse reaction is comparatively less likely? Even more importantly, could a physician legitimately exclude all his Caucasian patients from receiving the medication, knowing that there would be a 46% chance of their exhibiting the normal drug-metabolizing phenotype? Race's predicative power in individual drug response has thus been called into question, and cannot wholly be upheld by even its staunchest supporters or most obvious examples.

There are other important obstacles involved in clinically implementing race-based pharmacogenetics. Many critics have, for good reason, pointed to the inherent problems encountered when dividing the entire population into 5 major ethnic groups, claiming that classification would be especially difficult in the US population because it is extremely heterogeneous—a genetic melting pot that parallels the popularly identified cultural one. Schwartz argues that racial classification is useless in treating a patient, citing that on the 2000 US Census almost 7 million people identified themselves as members of more than one race. "After 400 years of social disruption, geographic dispersion, and genetic intermingling," he states, "there are no alleles that define the black people of North America [for example] as a unique population or race"[16]. Other researchers, however, assert that despite popular beliefs, ethnic groups within the US population have, to a large extent, remained endogamous. Risch, et. al. use the same 2000 US Census report to indicate that Schwartz's data is misleading. The 7 million people to whom he refers only represent a tiny fraction (2.4%) of the US population; 97.6% of citizens reported themselves to belong to a single race[14]. Both Risch, et. al. and Burchard, et. al. use gene flow data to state that despite minor admixture, African Americans, Asians, Pacific Islanders, Native Americans, and even Caucasians have retained most of their indigenous origins. For example, genetic studies of black Americans, perhaps one of the most heterogeneous racial group, have documented 7% to 20% white admixture depending on geographic location,

and have led some researchers to conclude that racial classification is a useful tool in even the most admixed of categories. Burchard et. al. therefore conclude that "black Americans, as a group, are still genetically similar to Africans." Again, the extent to which group-based data can apply to individuals is unclear, and this problem becomes amplified when attempting to classify multiracial individuals, especially Hispanics, who were included in the "other" category on the US Census because they are of mixed white, Native American, and African ancestry. Although a rough estimate of Hispanic ancestral proportions can be determined based on region of origin, even Risch et. al. admit that "individuals of mixed ancestry...will not be easily categorized by any system of finite, discrete categories." [14, 20]

Therefore, several inherent problems emerge when using population-based data to predict individual genetic make-up for clinical applications. Although pharmacogenetics intends to improve the availability of drugs by tailoring them to specific subgroups within a population, we can see that race-based classification may in fact undermine these intentions because it would inherently utilize the same elements of likelihood and generalization as current "one-size-fits-all" methodology. Critics often use these ambiguities to insist that race should be completely abandoned because it is too broad a stratification tool and therefore "of no proven value in treating a patient"[16], citing individual genotyping as a more specific and personalized methodology. However, these critics often fail to realize that, like race-based classification, individual genotyping does not eliminate any elements of guesswork; guesswork will always be involved in pharmacogenetics, even if individual genotypes can be ascertained. Lindpainter states, "all diagnostic approaches ultimately provide only a measure of probability, not of certainty."[9] Lipton also cautions that genetic tests will usually not reveal a simple status of either "responder" or "nonresponder," but rather a likelihood of response that may prove to be unhelpful in making pharmacogenetic decisions[13]. Unlike race-based classification, however, individual genotyping was previously shown to be impractical and lack sufficient consideration for environmental variables. Given all currently available alternatives and technology, it can be concluded that individual genotyping is inferior to race-based classification. Although crude, it is the most practical manner in which clues to drug response can be obtained and pharmacogenetic inferences made. Karter states that "epidemiologists have a long history of benefiting from designs that stratify samples in rather crude categories...despite [their] imperfection[s]," and concludes that "the use of self-identified race...may be the only practical way [we can fill] large gaps in our understanding [of drug response]"[11]. In an editorial in *The New England Journal of Medicine*, Dr. E. G. Phimister elucidates the usefulness of race-based classification most eloquently:

> In the meantime, we are in a phase of discovery... It is because of the potential usefulness of gene variants in...targeting therapies that the quest for genes that underlie complex traits continues. The goal of personalized medicine is...the treatment of disease on the basis of a person's genetic profile—which would render biologic consideration of race obsolete. But it seems unwise to abandon the practice of recording race when we have barely begun to understand the architecture of the human genome and its implications for...the identification of gene variants that...modify the effects of drugs[30].

Racial classification therefore confers obvious advantages in the development and prescription of drugs. The joining of race and medicine is still an extremely contentious topic, however, and strong resistance to universally integrating it into both research and medicine is mainly based on social, not scientific, concerns. Even though they acknowledge that race can be a useful, practical, and scientifically relevant tool, many researchers worry about the potentially negative social consequences associated with widespread use. Schwartz suggests that "racial profiling" in medicine will harm the "bond of trust" between physicians and their patients[16]. Others have argued that physicians

are obligated by the Hippocratic oath to take advantage of every available clue to a patient's drug response[6]. There has also been speculation about the labeling of drugs approved for use by a single racial group, as in the case of NitroMed. Robert J. Temple, the associate director for medical policy at the FDA, stated that even though approving NitroMed's use by blacks would "simply [represent] an extension of the agency's current practice of including information [about] effectiveness or safety" within given segments of the population, he acknowledged that "wording the usage instructions would be tricky." The label would have to emphasize the "benefits found in blacks," yet make it clear that this suggestion does not exclude other racial groups[18].

It is undoubtedly true that the term "race" carries with it "the dead weight of its own noxious past"[21] and has received special attention because of "society's deplorable history of racism and eugenics"[11]. Cooper points out that our modern concept of race grew out of the Europeans' need to name and organize the populations encountered during their rapid imperial expansion, and has used this negative historical reference to claim that racial classification is "not a propitious beginning" for pharmacogenetics[17]. A countless number of examples have indeed been documented in which specific ethnic groups were placed at a disadvantage in terms of both the provision of health care and the methodology used by researchers. Critics often cite the Tuskegee Syphilis Experiment, during which syphilis infections in African American men and their families were intentionally left untreated for research purposes. They also cite the controversy over HeLa cells, which were used to develop the polio vaccine as well as "reinvigorate" the fields of tissue and cell biology—all without the African American woman from whom they were taken ever receiving sufficient recognition or compensation[1]. In fact, a recent Yale University study reported that both black and white doctors are far less likely to offer cardiac catheterization to black patients than white patients, leading Dr. David Williams, a University of Michigan sociologist, to conclude that "doctors have been socialized to view patients who are poor, or black, or both, as inappropriate candidates for certain high-tech procedures"[31].

To what extent would such "unconscious, unthinking" discrimination influence the availability of future pharmacogenetic drugs? In an article about pharmacogenetics' ethical implications, Lipton considers the possibility that race-based classification may exacerbate already existing inequalities, especially when the economic considerations of health care providers are taken into account. He speculates that certain medications may be preferentially developed over others "because…Caucasians…are a wealthier patient group than [other] individuals with the same [medical] condition"[13]. Other researchers caution that pharmacogenetics scientifically reaffirms current social hierarchies in which certain groups dominate over others, and is therefore inadvertently justifying racism[17]. Though these possibilities should not be overlooked, there are definitive ways in which they may be avoided. Paul and Roses have suggested that pharmacogeneticists must affirm their social responsibility by ensuring that the development of and access to novel medical applications applies to all social and ethnic groups[24]. It has also been suggested that before attempting to study correlations between racial and genetic differences, researchers must first demonstrate credible scientific reasons for believing such a link exists[16]. Whether these guidelines can or will be formally enforced, however, remains to be seen.

When studying the controversy surrounding race's pharmacological role, it becomes even more important to note that much of the negative reaction descending upon race-based pharmacogenetics revolves around a kind of sensationalism—on the part of both critics and the media. Although Cooper insists that geneticists are "using scientific ideas for their own social purpose[s]"[21], one would be hard-pressed to find a research paper in which such "social purposes" are outlined. In fact, many researchers seem to want to use their findings about genetic dose response differences to emphasize the need for efficacious drugs in underrepresented segments of the population. In their enalapril study, for example, Exner, et. al. are quick to point out that their results suggest "that the overall popula-

tion of black patients with heart failure may be underserved by current therapeutic recommendations"[27]. When studies such as these were subsequently reported in the media, however, results were often oversimplified and generalized, causing much more attention to be drawn to the study's ability to pinpoint genetic "deficiencies" in the entire black population rather than its usefulness in underscoring the need for specific pharmacological alternatives[3]. Paul and Roses assert that "as a result of media sensationalism..., public opinion is frequently dominated by an uninformed, generalizing...stance toward genetics-based research..., too often with little basis in fact"[24]. Therefore, it may not be the researchers who are using racial differences to justify their own social agendas, but rather the media that tends to distort the results of their studies.

Are this distortion and its possibly harmful side effects sufficient to merit the complete abandonment of race as a drug response indicator? Many of the most ardent critics think so. Former President Clinton has proclaimed that the "great truth" to emerge from the Human Genome Project is the fact that "in genetic terms, all human beings, regardless of race, are more than 99.9% the same"[3], while critics of using "racial profiling" in medicine insist that the Project was not intended to reinforce genetic differences, but rather to reaffirm that "in medicine, there is only one race—the human race"[16]. However, it doesn't require much thought to realize that the very same critics who scorn pharmacogeneticists for attempting to achieve some vague "social purpose," are also attempting to align scientific findings with their own social ideals—those of absolute and complete equality.

Paul and Roses state that in attempting to move towards (perhaps unreachable) social ideals, "public discourse and decision making [can yield] results that are inconsistent with rational health care"[24]. Although many critics seem to suggest that relinquishing the specificity of race-based classification for traditional "one-size-fits-all" techniques will hasten the equalization of minority populations, ignoring inexorable and deep-rooted genetic differences—even if they represent only 0.1% of the human genome—will put the very same minority groups at an extreme disadvantage. Any US study that randomly samples subjects without regard for race will obtain roughly 75% Caucasians, 12% African Americans, 12% Hispanics, and 4% Asians, with little to no Native Americans or Pacific Islanders. Results from recent race-blind studies have thus been largely derived from the Caucasian majority and have inadequately sampled minority populations[14]. In studies in which important racial differences may exist, such as those dealing with large-scale trials of heart failure treatments, differences in drug response would neither be discovered nor explored. Researchers would miss opportunities to develop appropriate interventions in groups that direly need them[20, 27].

Implementing race-based classification as a drug response profiling tool is the only way in which pharmacogenetics can effectively be integrated into medicine. Researchers and health care providers may not only be ethically obligated to personalize medicine by taking advantage of racial diversity in drug response, but are scientifically justified in doing so. The only considerable barriers to personalizing medicine are the dearth of pharmacogenetic information and the public's need to recognize that these findings are both socially constructive and scientifically appropriate. "What is not scientific," state Risch, et. al., "is a [racist] value system attached to any such findings"[14].

Editor's Note:

If you are interested in reading more about this topic, please see Dr. Saly Satel's article about the importance of race in differential diagnosis. Published in *The New York Times,* May 5, 2002.

http://www.sallysatelmd.com/html/a-nytimes3.html

Several different viewpoints on racial and ethnic disparities in medicine are available in the 2001 issue of the *Yale Journal of Heath Policy, Law, and Ethics.*

http://www.yale.edu/yjhple/previous_links.html

Author Biography

Hilary Glazer is a sophomore at Tufts University majoring in Biology and possibly Spanish. She is interested in cellular and molecular biology and hopes to attend a combined MD/PhD program after graduating, ultimately becoming a researcher-physician in a highly specialized biological and medical field. She also hopes to learn to speak Spanish fluently.

References

[1] *The Human Genome Project and Minority Communities: Ethical, Social, and Political Dilemmas.* Zilinskas, R. A. and Balint, P. J. (eds) Praeger, pub. Connecticut (2001) pp. 35, 37-38, 72.

[2] Holtzman, N. A. and Marteau, T. M. (2000) "Will genetics revolutionize medicine?" The New England Journal of Medicine **343** (2): 141-144.

[3] Boyce, N. All the difference in the world. U.S. News and World Report. November 11, 2002: Science and Technology.

[4] Kalow, W. (2001) "Pharmacogenetics, pharmacogenomics, and pharmacobiology" Clinical Pharmacology & Therapeutics **70** (1): 1-4.

[5] Pirmohamed, M. (2001) "Pharmacogenetics and pharmacogenomics" British Journal of Clinical Pharmacology **52**: 345-347.

[6] C. I. Barash. Ethical Issues in Pharmacogenetics. 2001. http://actionbioscience.org/genomic/barash.html accessed November 14, 2003.

Barash, a trained philosopher with over twenty years of experience in health care, is the founder and principal of Genetics, Ethics & Policy Consulting, Inc., and was previously the director of a study on genetic discrimination funded by the Department of Energy. She wrote this article for BioScience Productions, Inc., an organization that promotes bioscience literacy.

[7] Kalow, W. (2002) "Pharmacogenetics and personalised medicine" Fundamental and Clinical Pharmacology **16**: 337-342.

[8] Wood, A. J. J. (2001) "Racial differences in the response to drugs—pointers to genetic differences" The New England Journal of Medicine **18**: 1393-1395.

[9] Lindpainter, K. (2002) "The impact of pharmacogenetics and pharmacogenomics on drug discovery" Nature Reviews: Drug Discovery **1**: 463-469.

[10] Evans, W. E. and Relling, M. V. (1999). "Pharmacogenomics: translating functional genomics into rational therapeutics" Science **286**: 487-491.

[11] Karter, A. J. (2003) "Commentary: race, genetics, and disease—in search of a middle ground." International Journal of Epidemiology **32**: 26-28.

[12] *Pharmacogenetics.* Weber, W. W. Oxford University Press, pub. New York (1997) pp. 3-4.

[13] Lipton, P. (2003) "Pharmacogenetics: the ethical issues" The Pharmacogenetics Journal **3**: 14-16.

[14] Risch, N. et. al. (2002) "Categorization of humans in biomedical research: genes, race, and disease" Genome Biology **3** (7): 1-12.

[15] Wilson, J. F. et. al. (2001) "Population genetic structure of variable drug response" Nature Genetics **29**: 265-269.

[16] Schwartz, R. S. (2001) "Racial profiling in medical research" The New England Journal of Medicine **344** (18): 1392-1393.

[17] Cooper, R. S. (2003) "Race and genomics" The New England Journal of Medicine **348** (12): 1166-1170.

[18] Cha, A. E. Race plays a new role in drug trials; treatment by genetic origin, ethnicity divides medical profession. The Washington Post. July 28, 2003: 1.

[19] *Pharmacogenetics of Drug Metabolism.* Kalow, W. (ed) Pergamon Press, pub. New York (1992) pp. 121-134, 871.

[20] Burchard, E.G. et. al. (2003) "The importance of race and ethnic background in biomedical research and clinical practice" The New England Journal of Medicine **348** (12): 1170-1175.

[21] Cooper, R. S. (2002) "Race, genes, and health—new wine in old bottles?" International Journal of Epidemiology **32**: 23-25.

[22] Feldman, M. W. et al (2003) "A genetic melting-pot" Nature **424**: 374.

[23] Editorial. (2001) Nature Genetics **29**: 239-240.

[24] Paul, N. W. and Roses, A. D. (2003) "Pharmacogenetics and pharmacogenomics: recent developments, their clinical relevance and some ethical, social, and legal implications" Journal of Molecular Medicine **81**: 135-140.

[25] Xie, H. et. al. (2001) "Molecular basis of ethnic differences in drug disposition and response" Annual Review of Pharmacology and Toxicology **41**: 815-850.

[26] Yancy, C. W. et. al. (2001) "Race and the response to adrenergic blockade with carvediol in patients with chronic heart failure" The New England Journal of Medicine **344** (18): 1358-1365.

[27] Exner, D. V. et. al. (2001) "Lesser response to angiotensin-converting-enzyme inhibitor therapy in black as compared with white patients with left ventricular dysfunction" The New England Journal of Medicine **344** (18): 1351-1357.

[28] Rosenberg, R. Firm to test heart drug specifically for blacks: NitroMed hopes for major impact on high-risk population. Boston Globe. March 10, 2001: F1.

[29] Reed Business Information, Ltd. Race has no use in matching treatments: geneticists. Pharmacy News (Australia). August 11, 2003.

[30] Phimister, E. G. (2003) "Medicine and the racial divide" The New England Journal of Medicine **348** (12): 1081-1082.

[31] Stolberg, S. G. The world: skin deep; shouldn't a pill be colorblind? The New York Times. May 13, 2001: D1.

TuftScope
The Interdisciplinary Journal of Health, Ethics, and Policy
April 2004 Volume 4

EXAMINING ENVIRONMENTAL JUSTICE

Joel Cohen

Since the mid-1980's there has been an increasing public awareness that the environmental hazards across the country are disproportionately distributed in communities of color and low socioeconomic status. Numerous studies have shown that these groups generally live closer to and are disproportionately exposed to facilities for treatment or disposal of hazardous material, polluted industrial facilities, and landfills[4]. Environmental policies of numerous corporations have targeted these groups as sacrificial populations. It is important to note that environmental justice's involvement in such politically charged issues as racism and classism has spurred arguments for and against the very existence of environmental injustice, and the need to measure and remedy any harm caused.

Such contradicting responses from the political and scientific communities emphasize the fact that issues of environmental justice involve far more than just the unequal exposure of minority or low socioeconomic groups to environmental health risk. Concern about environmental justice stems from the lack of participation of some communities in environmental policy and decision-making process, and "the very serious asymmetry of governmental and private-sector response to the environmental concerns and demands of minority and low-income communities"[4]. In other words, calculating the distribution for risk of environmental harm in terms of environmental justice must involve the assessment of a number of variables including race, class, and other factors affecting the likelihood for political mobilization for a particular community[3].

The complexities of environmental justice range from difficulties in performing sound, objective scientific research to developing reasonable and effective legislation. In order to develop any kind of policy to address environmental justice, it is necessary to understand the potential problems in research that attempts to prove the existence of environmental injustice. These include: limitations in the ability to generalize certain study models such as case-studies and difficulties in selecting representative population groups, distinguishing between correlative and causal relationships, and achieving true objectivity in scientific research.

Once the significance and validity of relevant environmental justice studies are established, politicians can formulate legislation that will most effectively address problems of environmental justice. For example, Democratic presidential contender Senator John F. Kerry has proposed the establishment of environmental empowerment zones that would address the remediation and prevention of future environmental injustices. The environmental empowerment zones would be modeled after economic empowerment zones, with development decisions subjected to federal and local scrutiny about their impact on communities. Without legislation regulating the distribution of environmental hazards, environmental injustices will continue to plague minority, low-income populations, thereby perpetuating a culture of racism and classism.

Since the mid-1980's there has been an increasing public awareness that the environmental hazards across the country are disproportionately distributed in communities of color and low socioeconomic status. Numerous studies have shown that these groups generally live closer to and are disproportionately exposed to facilities for treatment or disposal of hazardous material, polluting industrial facilities, and landfills[4]. Environmental policies of numerous corporations have targeted these groups as sacrificial populations. This is quite evident in cases as early as the 1984 report of Cerrell Associates to the California Waste Management Board. In the report, entitled "Political Difficulties Facing Waste-to-Energy Conservation Plant Siting," the conclusion reads:

> All socioeconomic groupings tend to resent the nearby siting of major facilities, but middle and upper socioeconomic status possess better resources to effectuate their opposition. Middle and higher socioeconomic strata neighborhoods should not fall within the one-mile and five-mile radius of the proposed site[8].

The report also stipulates that target communities should include those of populations less than 25,000, be rural, politically conservative, above middle age, with high school or less education, those with low income, and those who are likely to benefit from jobs provided by the waste industry if a plant is built in their community[8]. Similar policies have been developed across the United States, thereby unequally distributing environmental hazards posed by waste dumps.

In addressing these issues the Environmental Protection Agency (EPA) has defined environmental justice as the fair treatment and meaningful involvement of all people regardless of race, color, national origin or income with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies. Fair treatment means that no group of people, including a racial, ethnic or socioeconomic group, should bear a disproportionate share of the negative environmental consequences resulting from industrial, municipal, and commercial operations or the execution of federal, state, local, and tribal programs and policies. Meaningful involvement means that (1) potentially affected community residents have an appropriate opportunity to participate in decisions about a proposed activity that will affect their environment and/or health; (2) the public's contribution can influence the regulatory agency's decision; (3) the concerns of all participants involved will be considered in the decision making process; and (4) the decision makers seek out and facilitate the involvement of those potentially affected[11].

Environmental justice's involvement in such politically charged issues as racism and classism has spurred arguments for and against the very existence of environmental injustice, as well as the need to measure and remedy any harm caused. For example, writer and social analyst David Friedman denies the existence of environmental racism; he argues that the environmental justice movement is a government-sanctioned political ploy that will hurt urban minorities by driving away industrial jobs. In his article, "The Environmental Racism Hoax," he writes:

> The agency claims that state and local policies deliberately cluster hazardous economic activities in politically powerless "communities of color." The reality is that the EPA, by exploiting every possible legal ambiguity, skillfully limiting debate, and ignoring even its own science, has enshrined some of the worst excesses of racialist rhetoric and environmental advocacy into federal law[5].

Friedman suggests the environmental justice movement has been greatly exaggerated through biased science and the provocative nature of a racist debate. He feels overall that the movement has led businesses to simply redline minority communities and shift operations to areas inhabited by more politically conservative and white populations rather than risk costly lawsuits or EPA scrutiny. Such contradicting responses from the political and scientific communities emphasizes the fact that issues of environmental justice involve far more than just the unequal exposure of minority or low socioeconomic groups to environmental health risk. Concern about environmental justice stems from the lack of participation of some communities in environmental policy and the decision-making process, and "the very serious asymmetry of governmental and private-sector response to the environmental concerns and demands of minority and low-income communities"[4]. In other words, calculating the distribution for risk of environmental harm in terms of environmental justice must involve the assessment of a number of variables including race, class, and other factors affecting the likelihood for political mobilization for a particular community[3]. This paper examines two issues in environmental justice: (1) common pitfalls

and limitations in the scientific methodology that forms a basis for environmental justice arguments; and (2) the political implications of environmental justice in terms of future policymaking.

Limitations in Environmental Justice Science

As stated earlier, a minimalist conceptual model for evaluating the distribution of environmental harm must include three independent variables: race, class, and political mobilization. Researchers use a number of different methods for gathering and deciphering appropriate data. Within these methodologies there are a number of potential limitations and pitfalls that could raise doubts about the validity of environmental injustice. This paper discusses limitations in study models, data collection, correlative vs. causal relationships, and difficulties in assessing and/or achieving objectivity in environmental health research (with a case-study of the Three Mile Island incident). It is necessary to be aware of these limitations in order to (a) promote proper scientific models for environmental justice research, ensuring unbiased and accurate data collection; and (b) skillfully interpret data from previous studies so as not to be tricked by manipulative language or incorrect conclusions. While a number of studies have in fact addressed these limitations and produced useful conclusions and suggestions, the potential danger of a highly publicized but poorly conducted study makes it an issue worth discussing.

1. Stud Models

Most early environmental justice studies have used a case-study model for collecting data. From these studies researchers have made sweeping generalizations about environmental injustices across the country and a need for change in policies that systematically propagate environmental racism. Case studies are indeed a valuable research method, but they are inherently limited in their ability to generalize their findings to any population outside of the one studied[3]. If a researcher finds that in Alabama blacks are six times more likely than whites to be living near toxic waste dumps, this finding cannot necessarily be extended to blacks elsewhere in the United States. In order to support a broader generalization, one must perform a meta-analysis of several case-studies, comparing all of their results and using them to make a larger conclusion such as: across the United States, blacks are more likely than whites to be living near toxic waste dumps.

2. Data Collection

An additional problem with research on environmental justice involves the selection of geographic areas for study. There is a substantial amount of literature that focuses on ZIP code areas and proximity to specific environmental hazards[3]. However, this strategy fails to acknowledge the fact that post offices lack the ability to systematically distribute environmental hazards unequally across race. When researching specific geographical areas it makes more sense to study states, counties and cities—areas that have governmental bodies that could potentially be held accountable for environmentally unjust policies[3]. While collecting data on states, counties, and cities ensures a relationship between specific policies and the resultant distribution of environmental exposure, the data are likely to contain aggregation errors or bias that can mask exposure patterns[3]. For example, studying environmental exposure across the state of Vermont may overlook trends that occur on a smaller, neighborhood scale. In most scientific studies there is an inherent tradeoff between aggregation problems (variations within the regions of analysis) and the availability of data[3]. It is therefore necessary to either study a population or geographical area large enough to include the effects of environmental hazard exposure yet small enough to record significant socioeconomic variation, or recognize and make clear the limitations in data gathered from either a microscopic or macroscopic population.

3. Correlative vs. Causal

It is important to note that studies investigating the distribution of environmental hazards across the variables of race, income and likelihood for political mobilization simply establish correlative rather than causal relationships. In their work entitled *From the Ground Up*, Luke Cole and Sheila Foster examine this issue while attacking

the views of some environmental justice skeptics: "Some commentators therefore question whether the misdistribution of environmental hazards is appropriately attributed to racism or other injustice or to a more benign explanation"[6]. Cole and Foster recognize one common alternative explanation for the unequal distribution of environmental hazards suggesting it is the result of the social status or lifestyle choices of certain racial and ethnic groups. This model essentially frames disproportionate exposure to environmental hazards as a choice those exposed have to make, such as the choice to live in metropolitan areas (thereby increasing likelihood of exposure to waste dumps) or the choice of undocumented Latino immigrants to work on farms (increasing exposure to toxic pesticides)[6]. However, this model overlooks social processes and institutions that funnel various groups into their current situations, and incorrectly suggests the possibility that exposure to environmental hazards is a lifestyle choice that can be changed and therefore remedied. While Cole and Foster emphasize this theory's innate flaws, they use it as an example to emphasize the fact that scientific research on environmental hazard distribution can only give us correlations, and do not tell us why certain inequities exist.

4. Objectivity
(Case Study: Three Mile Island)

Research into most environmental justice issues involves many stakeholders, each with differing and often conflicting interests. For example, a local political figure may oppose research that exposes his policies as allowing toxic waste to be dumped in a predominantly minority neighborhood. Large corporations responsible for illegal emissions practices or unfairly distributed environmental harms do not want scientific research to result in expensive lawsuits. Families want science to prove that the metallic taste in their tap water comes from chemicals dumped in the nearby river and is noticeably increasing cancer rates in children. Research can easily be biased to favor any one of these sides, resulting in contradictory studies examining the same situation. While large companies and governments have the ability to make significant environmental impacts as well as sponsor research on those impacts, the families or small communities that are most directly affected usually have neither political power nor the capacity to conduct research to document their exposures or health conditions[10]. What emerges is research sponsored and framed by those that have an economic or political interest in the results. Even if local communities can raise enough funds to conduct a study of their own, their research also has the potential for bias if its focus is to prove the existence of some environmental hazard.

Scientific objectivity is commonly thought of as the "consequence of standardized methods of quantitative observation and experimentation. The scientific method, by removing subjectivity and social influence, yields knowledge that is ostensibly trustworthy and objective"[10]. When reviewing environmental justice research it is necessary to recognize that science is not always the objective observer it claims to be. Rather, "science is molded by society because it is a human productive activity that takes time and money, and so is guided by and directed by those forces in the world that have control over money and time"[1].

An example in which different stakeholders affected the kind of science performed to assess an environmental hazard involved an incident at a nuclear facility on Three Mile Island, Pennsylvania in 1979. In the early morning of March 28, 1979, the nuclear plant lost control of one of its reactors, resulting in uncontrolled releases of radiation to the surrounding environment for several days. Malfunctioning and overloaded monitors were unable to measure exactly how much radiation had been released. Soon after the incident, many local residents reported such conditions as "metallic taste, erythema, nausea, vomiting, diarrhea, hair loss, deaths of pets and farm and wild animals, and damage to plants," all of which are common symptoms associated with exposure to radiation[2]. Four years later residents reported 19 cancer deaths during 1980-1984, much high than their annual average of 2.6[10]. In 1981, a study financed by the nuclear industry began examining cancer rates ranging from 1975-1985, looking for a relationship between the estimated radiation

exposure and cancer incidence. The results were published in two studies released in 1990 and 1991 that concluded there was no convincing evidence that Three Mile Island radiation releases had influenced cancer in the area[10].

By the time these studies were published, a lawsuit involving 2,000 plaintiffs claiming health damages from radiation released in the Three Mile Island incident had been under way for several years. The plaintiffs argued that emissions of radioactive gases during the accident were much larger than had been estimated by nuclear industry and governmental officials. Furthermore, meteorological conditions and hilly terrain had caused the radioactive gases to disperse into narrow columns, intense clouds of gas that exposed small areas of the surrounding countryside to high radiation doses, resulting in health impacts including heightened cancer rates[9]. When the studies' results were presented in court, the plaintiffs initiated a reanalysis of the data previously gathered. The new study found a number of methodological problems with the one funded by the nuclear industry. For example, the counts for leukemia were unnecessarily arranged, thereby weakening the data. Although the industry study included leukemia as a primary outcome, incidence among children and adults had been analyzed separately, reducing already small sample sizes. Moreover, the childhood cancer analyses considered children born after the accident, potentially diluting further any differences in the cancer outcomes between exposed and non-exposed. After accounting for these problems, the new study found there was in fact a positive relationship between accident dose estimates and cancer rates[9].

An analysis of these studies by Steve Wing suggests additional problems with the original study's hypothesis. Sound scientific research requires a testable hypothesis, or a situation where evidence on the studied effect can be interpreted as supporting or disproving the hypothesis. The industry-financed study looked for an association between cancer rates and the exposure levels estimated by industry and government officials. First, the plaintiffs claimed that the officials underestimated the levels of radiation exposure, and that the true levels were high enough to cause an observable increase in cancer rates. Second, the original study stated outright that the accident doses were too low to produce the effect hypothesized. Therefore, "assumptions of low doses clearly precluded an interpretation of the positive dose-response relationships as supportive of the hypothesis under investigation"[10].

Wing considers issues of objectivity a great hindrance to the science of environmental justice, and suggests a method for a self-aware science that understands its own assumptions as well as the limitations posed by them.

> Strong objectivity demands that scientists critically evaluate how the knowledge they create is shaped at every point by historical social forces…Scientists should be trained to engage in careful reflection about how the history of their discipline has affected their hypotheses, assumptions, and tools, and how their work, like the work of others before them, is shaped by contemporary forces…Strong objectivity is needed, not only for good science, but for ethical conduct of research[10].

Wing's vision for a self-critical science addresses the very serious issue of objectivity in environmental justice research. In a field littered with conflicting players of varying economic and political clout, strong objective science is absolutely necessary to avoid the kind of mistakes made in research on the Three Mile Island incident.

Policy

Given the extreme complexity surrounding the environmental justice issue in terms of both its cultural implications and the problems surrounding scientific research, any policy addressing the issue must be elastic enough to allow for modification and objectivity, but stringent enough to effectively remedy any situation where true injustices occur. Edwardo Lao Rhodes suggests some guiding principles for developing environmental justice policies at any level of government in his book Environmental Justice in America. He first stipulates that

any policy must promote conditions that provide opportunities for fair and equal participation by all parties affected by environmental hazards in the policy surrounding those hazards. This is an interesting point as it allows groups potentially affected by an environmental hazard a sort of negotiation right; if they are going to be burdened with the hazard, they can guarantee themselves some sort of compensation within the regulative policy concerning the hazard. Secondly, such policies must address the "remediation, compensation, and redistribution of inequities in burdens and benefits"[4]. This principle is absolutely necessary in a proposed policy as remediation, compensation, and redistribution of inequities are the first steps towards correcting any environmental injustice. Lastly, environmental justice policy must avoid forcing a "paternalistic" outcome on the affected parties[4]. Rhodes argues that a paternalistic outcome would be "to replace one form of injustice with another," or to replace the injustice of environmental racism with the injustice of unfair over-regulation of businesses[4]. His final point merely reminds policymakers of the dangers of enforcing unreasonable regulations.

Rhodes' principles are a step in the right direction for developing effective environmental justice legislation in that they address the need for policy to ensure a fair distribution of power, corrective action and fair punishments. However, Congress has yet to pass legislation specific to environmental justice despite several attempts from 1992 to 1996[3]. During the last decade, the EPA has established a number of subcommittees and organizations with vaguely defined responsibilities such as ensuring the incorporation of environmental justice issues in important decisions and policy development, with the hopes of jumpstarting environmental justice legislative proposals.

In 1992 the EPA created the Office of Environmental Justice to coordinate the agency's efforts to address the environmental justice issue. Each region and headquarters office was asked to appoint an Environmental Justice Coordinator specifically responsible for ensuring that environmental justice is included in policy input, program development, and implementation. The Policy Working Group was formed to ensure that "cross-media policy development and coordination occurs at all levels"[12]. The Executive Steering Committee was established to provide leadership and direction on policy planning. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations", was signed by President Clinton February 11, 1994, to ensure federal attention on environmental injustices occurring disproportionately in minority and low-income populations. To ensure that the EPA is open to input from the variety of stakeholders involved in environmental justice issues, the National Environmental Justice Advisory Council (NEJAC) was established. The purpose of this group is to provide consensus advice on a variety of documents, including the EPA's Environmental Justice Agenda, and the Environmental Justice Annual Report. The NEJAC meets 2-3 times a year throughout the country to receive comments from local citizens and community groups on the state of the environment in local areas.

Finally, two grant programs assist communities and tribal governments in addressing local environmental concerns. The EJ Small Grants Program, established in 1993, provides financial assistance to community-based organizations working on solutions to environmental problems within their community. Community groups can use this money to assess the environmental damage done to a site, to cleanup a polluted site, or even to pay for legal advice on environmental justice lawsuits. In 1995, the Community-University Partnership was created. This program offers up to $300,000 to local communities working in active partnerships with nearby universities and colleges on local environmental justice issues[12].

Although there have been some broad-based environmental justice legislation proposed during the early 1990's, there has been little federal legislative action or prospect for action in the near future[4]. However, a plan proposed by Democratic presidential contender Senator John F. Kerry offers a glimmer of hope for the remediation and prevention of environmental injustices. In a speech at the Vine Street Community Center in Roxbury, Massachusetts last April, Kerry called

for the establishment of "environmental empowerment zones," and a new system for tracking child asthma and other diseases linked to environmental factors[7]. The environmental empowerment zones would be modeled after economic empowerment zones, with development decisions subjected to federal and local scrutiny of their impact on communities. The proposed disease-tracking system would be implemented by an environmental health officer in each state who would coordinate disease and pollution data annually[7]. Little groundwork has been laid for addressing environmental justice issues, and proposals such as Senator Kerry's environmental empowerment zones and disease tracking systems are necessary to effectively manage disproportionate distributions of environmental hazards.

Conclusion

The complexities of environmental justice range from difficulties in performing sound, objective scientific research to developing reasonable and effective legislation. In order to develop any kind of policy to address environmental justice, it is necessary to understand the potential problems in research that attempts to prove the existence of environmental injustice. These include: limitations in the generalizability of study models such as case-studies and difficulties in selecting representative population groups, distinguishing between correlative and causal relationships, and achieving true objectivity in scientific research.

Once the significance and validity of relevant environmental justice studies are established, however, legislation such as the environmental empowerment zones proposed by Senator Kerry can be considered and eventually modified and/or implemented. The EPA has recently reinforced its hard-line stance on environmental justice; an August 2001 memorandum from Administrator Christine Todd Whitman recommitted the agency to "integrating environmental justice into all agency programs"[11].This is a significant initiative, for without legislation regulating the distribution of environmental hazards, environmental injustices will continue to plague minority, low-income populations, thereby perpetuating a culture of racism and classicism.

Author Biography

Joel Cohen is a senior at Tufts University triple majoring in Anthropology, Environmental Studies, and Community Health. This article was originally a paper written for his Bio97: Contemporary Biosocial Problems class. He would like to thank Dr. Ross Feldberg for his help and encouragement with the original draft.

References

[1] *Biology as Ideology: The Doctrine of DNA*. Lewontin, R. HarperPerennial, pub. Ontario (1993) pp. 3.

[2] Del Tedici, R. (1980) "The people of Three Mile Island" San Francisco, CA: Sierra Club.

[3] *Environmental Injustice in the United States: Myths and Realities*. Lester, J. P. et. al. Westview Press, pub. Colorado (2000) pp.16-41.

[4] *Environmental Justice in America: A New Paradigm.* Rhodes, E. L. Indiana University Press, pub. Indiana (2003) pp.6-10, 180-190.

[5] Friedman, D. (1998) "The environmental racism hoax" American Enterprise Nov.-Dec.

[6] *From the Ground Up: Environmental Racism and the Rise of the Environmental Justice Movement.* Cole, L. K. and Foster, S. R. New York University Press, pub. New York (2000) pp. 50-60.

[7] Johnson, G. "Kerry to press 'environmental justice': seeks federal scrutiny and more oversight in minority communities." The Boston Globe. April 22, 2003: A2.

[8] *Killing Me Softly: Toxic Waste, Corporate Profit, and the Struggle for Environmental Justice.* Girdner, E. and Smith, J. Monthly Review Press, pub. New York (2002) pp. 53-60.

[9] Merwin, S. et. al. (2001) "Application of the Supreme Court's Daubert Criteria in radiation litigation" Health Physics **81**: 670-677.

[10] Wing, S. (2003) "Objectivity and Ethics in Environmental Health Science" Environmental Health Perspectives **111** (14): 1809-1818.

[11] Environmental Protection Agency (EPA). Environmental Justice. 2003. http://www.epa.gov/compliance/environmentaljustice/index.html

[12] Environmental Protection Agency (EPA). Environmental Justice Fact Sheet. 1998. http://www.epa.gov/compliance/resources/publications/ej/fact_sheet_ej_98.pdf

Correspondence

HRT: A Response

Lee Rubin

To the editors of TuftScope:

As a publication focusing on the intersection of humanism and bioethics within the context of modern medical science, TuftScope is an excellent place for the publication of Kate Gluckman's essay, entitled "Hormone Replacement Therapy: The end of the fountain of youth."[1] The author has put together a timely and valuable piece of work for TuftScope by utilizing retrospective analysis to examine the complex topic of hormone replacement therapy (HRT), with particular regard to the history and marketing of this treatment to women since the original release of Premarin in 1942. In response to her essay, I hope to clarify and expand on a few points of interest raised by the author.

First, it should be noted that the availability of true, long-term study data were not initially available for HRT or any other new drug placed on the market. Although the United States Food and Drug Administration (FDA) requires a series of clinical trials prior to approval of a new pharmaceutical agent, all medications released for public use are carefully studied for many years after their release because rare side effects are only observed once a drug is available to many millions of patients.

For example, salicylic acid, an active substance in plants used historically for thousands of years, was first synthesized for pharmaceutical use by Kolbe in Germany in 1874. Bayer modified the compound to acetylsalicylic acid and introduced the new drug as "aspirin" in 1899, hailing the compound for its analgesic, antipyretic, and anti-inflammatory properties.[2]

Today, 105 years later, despite having a multitude of beneficial uses and clinical indications, aspirin's "long-term" study data in the general population include a dramatic side effect profile featuring aspirin-induced asthma, dermatitis, gastritis, intestinal ulceration and perforation, renal toxicity, hemorrhage, and anaphylaxis. In fact, the "Reye's Syndrome" associated with aspirin use in children following a viral illness,[3] is a truly rare

aspirin side effect that was first described by Dr. R. Douglas Reye in 1963, a full 64 years after the drug became generally available. As this example demonstrates, the discovery of a medication's complete side effect profile is not often learned until decades after it is given to millions of patients.

The consideration above must force hesitation in considering the author's underlying assertion that sexism played a role in the advocacy of HRT use for women, realizing that HRT's elevation in risk for other serious diseases was unknown for decades. More likely than not, the driving force for the widespread usage of HRT from 1942 to 2003 was optimism, not sexism, on the part of physicians and the pharmaceutical industry in attempting to provide an improvement for the health of postmenopausal women.

Next, the author's accusation that "an inherently sexist and negative aura surrounding menopause and aging women" existed when HRT was introduced is doubtful. A review of the Random House Collegiate dictionary from 1968 finds the conspicuous absence of the terms "sexist" or "sexism," likely because these terms were introduced only as a result of the women's social revolution during the 1970's. In fact, a modern definition of "sexism," from www.dictionary.com,[4] defines the word in exactly this light: (1) Discrimination based on gender, especially discrimination against women. (2) Attitudes, conditions, or behaviors that promote stereotyping of social roles based on gender.

Gluckman's essay is a striking example of a modern, and a necessarily revisionist, view of medical history from the feminist perspective. If sexism was indeed inherent to society or the medical community during the middle decades of the 20th century in relationship to HRT, the author has failed to cite it directly. Nearly all of the paper's 24 references were published between 2000 and 2003, and the absence of primary literature citations from the period extending from 1942 to 1975 (the first medical article cited by the author) prevents any objective analysis within the paper. Clearly, the views expressed are those of a modern author viewing history through the looking glass of contemporary social enlightenment and with the hindsight of recently published long term HRT data.[5] In fact, had the Women's Health Initiative (WHI) study drawn an opposite conclusion in 2002, the author's argument would have fully collapsed without the support of source citations from earlier in the 20th century to objectively validate her presumptions. Impressively, regarding the ambiguity of a recent HRT advertisement, the author notes that, "As in many drug commercials, the product being sold is not mentioned, nor its purpose." In fact, such intentionally deceptive practices are often found in the direct-to-consumer (DTC) marketing of various pharmaceuticals. Misleading DTC advertising been placed under increasing federal scrutiny during the last five years, starting in 1999 when the FDA required ads to contain "these four sources: (1) a toll-free telephone number; (2) referral to a print advertisement in a concurrently running print publication, or provision of enough product brochures in various convenient outlets; (3) referral to a healthcare provider (physician, pharmacist, veterinarian or other healthcare provider); (4) an Internet web page address."[6]

Most recently, in August 2003, the FDA issued a policy statement that for DTC advertising to have a positive impact on patient/physician communications and best inform consumers, it must "effectively communicate not just the potential benefits of the advertised prescription drug, but also potential risks, such as those associated with drug interactions and the specific health condition of the individual considering taking the drug."[7] By requiring pharmaceutical companies to specifically state the drug's name, benefit, risks, and the condition it intends to treat, the FDA has taken great steps towards eliminating the type of deceptive advertisement Gluckman rightfully criticizes.

Overall, Gluckman's essay is a somewhat provocative analysis of the social and sexual implications of HRT over the last 6 decades, in the aftermath of the WHI study's blockbuster results in 2002. Certainly, this is a worthwhile perspective to include in *TuftScope*, although certain concepts and pitfalls from the essay are worthy of expanded analysis as described above.

Medical history is an interesting body of study, and only through retrospective analysis can one

attempt to understand how powerful marketing forces and social trends may have shaped the intentions of physicians and the treatment of patients over the course of time. This essay is entitled to a revisionist approach on the topic of HRT, and such a modern view serves as a timely reflection on the remarkable social evolution our society has experienced since Premarin was first introduced to women sixty-two years ago in 1942.

Respectfully Yours,
Lee Eric Rubin
Tufts University School of Medicine
Class of 2004

References

[1] Gluckman, K. (2004) "Hormone Replacement Therapy: The end of the fountain of youth" TuftScope **4** (2): 15-22.

[2] Vane, S.J. (2000) "Aspirin and other anti-inflammatory drugs" Thorax **55** (S2): S3-9.

[3] McGovern, M.C., Glasgow, J.F., and M.C. Stewart. (2000) "Reye's syndrome and aspirin: lest we forget" British Medical Journal **322** (7302):1591-1592.

[4] Dictionary.com. Sexism. 2004. http://dictionary.reference.com/search?q=sexism accessed March 11, 2004.

[5] Women's Health Initiative (WHI). (2002) "Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial" Journal of the American Medical Association **288** (13): 321.

[6] Food and Drug Administration (FDA). FDA issues final guidance for direct-to-consumer Rx drug advertisements. 1999. http://www.fda.gov/bbs/topics/ANSWERS/ANS00968.html accessed March 11, 2004.

[7] Food and Drug Administration (FDA). The Food and Drug Administration's Strategic Action Plan: Protecting and Advancing America's Health: Responding to New Challenges and Opportunities. 2003. http://www.fda.gov/oc/mcclellan/FDAStrategicPlan.pdf accessed March 11, 2004.

First Impressions of Medical Research: An Anecdotal Journal

Stephanie Albin

Introduction

Bellevue Hospital is the oldest public hospital in the United States, located in the lower east side of Manhattan in New York City. This is a hospital that prides itself on treating an incredibly diverse patient population. It is also the hospital that gave me my first real glimpse at life after medical school, of doctors putting knowledge into practice.

At Bellevue I helped conduct an observational study on the long-term psychological effects of September 11th and the Flight 587 Crash on urban Emergency Department (ED) patients. The study called for a survey of a random sample of around five hundred New Yorkers who may have been directly or indirectly affected by either disaster. The participating hospitals included the Center for Urban Epidemiological Studies (CUES), Columbia Presbyterian Medical Center, and Bellevue Hospital.

Each hospital has a different location and patient make-up. CUES is located in the New York Academy of Medicine and aims to foster the relationships between medical schools and health agencies. Columbia Presbyterian is located in Washington Heights and serves a majority of Dominican-born people, while Bellevue provides care to many immigrants, regardless of their racial and financial status.

My role in the study was essentially to gather raw data, through talking with patients and administering surveys in the emergency room. The following is an anecdotal journal of my experiences at Bellevue Hospital. The formal study was published in 2003.

The specific aims of the study were: (1) To identify the prevalence of psychological distress and Post Traumatic Stress Disorder (PSTD) among patients presented for care in an urban ED 9-12 months after the World Trade Center Disaster, and 7-10 months following the American Airline Flight 587 crash, in order to determine the association between severity of psychological symptoms and patterns of disaster event experiences, (2) to identify demographic and socio-economic correlates of chronic psychological distress and PSTD—such as social support, social networks, and social cohesion—several months post-disaster, (3) to identify specific groups at an increased risk of suffering psychological consequences from these disasters, and (4) to identify the prevalence and correlates of

smoking and alcohol use among ED patients after these disasters. (From *Determinants of Long-Term Psychological Sequelae in E.D. Patients Following the September 11th Terrorist Attacks and the American Airline Flight 587 Crash in N.Y.C.)*

My investigator and advisor was William K. Chiang, MD, from the Bellevue Hospital Center Emergency Department.

Entry One

After a wild goose chase to find the doctor I was working with for my project, I came to my first realization about doctors: they are extremely elusive. Common sense leads me to believe that their disappearing act is the result of over-committed scheduling and unexpected medical patients and emergencies. The shifts these doctors (and nurses) work are sometimes obscene: ten hours, twelve hours. I'm skeptical that any doctor *truly* had an hour free to talk to a Tufts sophomore about her future (and distant) medical plans and summer internship goals. It's funny how the introductions work here in the hospital; as soon as an employee heard which doctor I was "under the guidance of," it's almost as if my significance was suddenly realized. "Oh, you're doing research with Dr. Chiang! That's great, welcome!" So after hearing this approximately a dozen times, I had no choice but to conclude that my research experience *would* be great—that my efforts would contribute to both an informational and beneficial study.

The ED is split into two sections: urgent care and ambulatory emergency. I spent time with the patients in urgent care, those who were not critically ill and able to complete the survey comfortably. I began my tasks enthused and ended them disheartened. I came to my second realization of the day rather quickly: communication between doctors and their patients is incredibly important. This can be explained in two different ways. First, language barriers can create obvious problems, especially in a hospital such as Bellevue. The hospital has translators for every language imaginable, but Mandarin-speaking patients could not participate in a study that only offered surveys in only Spanish and English. Second, many patients understood English perfectly well, but chose to selectively hear what they wanted. Some patients were in the E.R. because they did not take medication properly or listen to the advice of previous doctors—the same people who declined participation in our study before even listening to my speech about its benefits and importance.

Out of a six-hour shift (and in accordance with the procedure to ensure random sampling of patients), I wound up recording one completed survey, one uncompleted survey, and six refusals to participate. I will admit that that some of this low patient participation may be due to the system employed by the hospital (more on this later if I have a more comprehensive view of the system and structure of the department), but I assume that operations move at approximately the same rate at any other hospital.

Entry Two

Whereas my last experience at the hospital was mostly observational, these past few days have been completely hands-on. All you need is one accommodating doctor, and you have full access to hospital operations. In this case, I was lucky enough to connect with an extremely intelligent and patient doctor, who basically took me under his wing for an entire shift.

We first interacted when a patient was admitted with an atypical chart (at least in my experience); a mental health institution had referred him for detox. This had been the first case to really peak my interest. Although lacerations, chest pains, and rashes are more frequent and occasionally exciting, this was an opportunity to see a patient with both a physical *and* a mental problem, a kind of social disorder. I asked the doctor for permission and actually observed two detox patients that day, one in for alcohol abuse and one in for crack-cocaine addiction. Both came in starved and tired, yet ready to trade street drugs for pharmaceutical drugs to regain some sort of normal life. I had a million questions to ask them, but found myself mute throughout the entire examination period. Once we left each room I unloaded a battery of questions upon the doctor, but never found the courage to ask these addicts directly about their backgrounds and problems. Each story affected me

rather deeply. The crack addict had been given his first taste of alcohol at age five, after his Rastafarian father began blowing marijuana smoke in his face at age four. All of this was shocking to me. The doctor, however, absorbed the information as if the patient were listing his family's history of arthritis. I guess in an urban neighborhood such as Bellevue's, stories such as these are a dime a dozen.

I think the doctor must have noticed my obvious curiosity and empathy for patients with more-than-physical problems and asked me if I wanted to help with some superficial examinations in the psychiatric ward. I had visited psych before, a day when they had gotten around ten new patients (all heavily sedated when I visited). The three people given physicals on this visit were not drugged, but surprisingly low-key for the ward. I soon figured out why. Two of the three patients were suffering from acute depression. One man was African, from Mauritania, and had a long history of depression and suicidal tendencies. The other patient was a nineteen-year-old African American girl with HIV. Her parents were both deceased, her mother from a drug overdose and her father from AIDS. The African man was soft-spoken yet stubborn about his impending mortality, as evidenced by blood in his stool. In fact, he was so concerned that he found it necessary to present a recent sample in a few sheets of paper towel. The African-American girl was quiet as well, but her eyes revealed some sort of inner devastation. Suddenly I felt horrible about my position at the hospital, something that I had never experienced before. I had observed many patients in the past, but I had never felt like a spectator watching a zoo display. What must this girl—my age, no less—think about a healthy peer observing and possibly judging her situation? I couldn't bear it, so I took a chance and started talking to the patient. We engaged in very superficial conversation, something about her shoes and their stylish soles. It wasn't much—we didn't make any kind of life-changing connection—but it was something. Surprisingly, it comforted me (and hopefully her) that she wasn't so different and we could find common ground. The third patient was a woman with paranoia who basically refused to talk honestly in front of me, convinced that I was there for malicious reasons. It was probably better this way; I had too many thoughts and emotions racing through my head to deal with another sad story. My compassion was abundant, but my ability to keep my own life a deserved reality rather than an unfair collection of advantages was waning.

Entry Three

After a usual day of working in urgent care, two major visions remained in my mind. Both were extremely significant and common in this environment, but one vision was much more subtle and commonly overlooked.

Vision one: two doctors conferencing about a particular patient, challenging and affirming each other's suspicions. Throughout another day of watching attending doctors (full-fledged, confident professionals), residents (practicing novices), and medical students (eager, bewildered academics), I noticed just how much doctors consult with each other before diagnosis and prescription of treatment. The medical students and most residents are required to present individual cases to the attending doctor, clearing all medical decisions before executing them. Knowing that a safety net of more experienced doctors will surround me during my first few years of actually practicing medicine was extremely comforting. But what about the one person who has the ultimate authority and is considered the full expert? What kind of pressure must a man or woman feel when a staff of five and a clinic of a hundred rest squarely on his or her shoulders?

I've come to recognize the high level of ambiguity and assumption involved in medicine. By this I mean the ambiguity of disease and injury and the assumption of accuracy in diagnosis—the latter of which is truly a hard pill for me to swallow. "Symptoms" is a term I've come to realize as a broad facilitator of diagnosis, but never a completely accurate definition of someone's affliction. To imagine that a doctor can identify and interpret all physical, biological, and chemical aspects of an illness is absurd, and unfortunately there is a great deal of overlap between the symptoms of diseases. This is probably the main cause of mis-

diagnosis, an indistinctness for which doctors are often blamed.

Emergency medicine requires a general, relatively brief knowledge of most departments of medicine. In essence, the emergency department is an organizational committee that deals only with immediate problems. They check to make sure a patient is stable at the present moment, try to alleviate any pressing discomfort with medication, and then direct them to the appropriate specialists. Personally, this seems a harder task than actually performing the needed procedure (i.e. surgery, therapy, etc.). Surgeons are highly specialized and trained in their fields and perform skills they have intently studied and practiced to perfection. Don't get me wrong—their jobs are far from easy—but a doctor's true accuracy and efficiency is more concretely tested in the emergency room. To be confident in a decision about someone else's health care is an impressive feat. (Even more impressive is the ability not to assign personal blame when alternate options could and should have been exercised.)

Vision two: an African-American male, approximately twenty-five, naked, with two small bullet holes seeping blood. When a doctor asked me if I would faint upon seeing a gunshot victim, I was quick to assure him of my strong tolerance of blood. I was partially correct in my statement; I did not faint, but I was not as stable as I thought I was would be. Nonetheless, the experience was incredibly interesting and satisfying.

Before I go on, let me digress and elaborate on the latter part of that statement with a personal truth: in my eyes, efficiency is one of the most valuable assets a person (or an organization) can have. After working at a pharmaceutical company for two weeks last winter, I realized that all the paper work the head of the department had me and around three other college students doing would be unnecessary if the company were to upgrade its electronic systems. I wanted to offer her some advice on running her company because it literally sickened me to have someone paying for mindless, completely avoidable tasks. It was a waste of their money and my time.

Now back to my experience at Bellevue. Unlike the pharmaceutical company, the medical team at Bellevue exhibited commendable efficiency in initially dealing with patients who faced potential death, such as the gunshot victim. I, however, experienced a kind of surreal sensation. It was as if my brain was incapable of completely registering what was happening before my eyes. I could intellectualize the condition of the man, but couldn't help but detach myself from emotionally recognizing just how close to death he had come. I still haven't decided what all of this means and whether that kind of detachment could negatively affect my ability to participate in a profession of service.

Entry Four

I feel more enlightened and useful at the hospital than ever before, probably because my day began with an abstract lecture and ended with a tangible application.

Project Health Care is a program run by Bellevue for both undergraduate and graduate students. Their job entails much of what I am currently doing: a combination of research and volunteer work in all departments of the hospital. They often have guest speakers come to the hospital, and today Dr. Marianne Legato from Columbia-Presbyterian Hospital came in. She came specifically to talk about her new book, Eve's Rib, a book which most volunteers had been required—err, I mean had opted—to purchase and read. The book supposedly outlines her progressive ideas about gender-specific medicine. She was an absolutely brilliant woman and impressed me with a very comprehensive speech about her ideas and efforts. In essence, Dr. Legato proposed that the differences between men and women are so great that medically, they should be approached and treated differently. She contended that the difference between the sexes spans much more than just reproductive organs. She outlined hormonal, skeletal, and anatomic distinctions, and heavily emphasized the dissimilar ways in which medical conditions manifest themselves in men and women.

I agreed with much of what the doctor stated, but was left with some reservations about her more radical ideas, as well as several doubts about her

professed motivation. Dr. Legato stated that a separation in medical approach and treatment for men and women was an absolute necessity. Some of her examples she used to support this claim, however, were entirely too unreasonable to win my support. She spent a great deal of time discussing her dissatisfaction with women centers throughout the country, categorizing them as "purple and pink departments that only perform mammograms and pelvic exams." She kept asking why these centers didn't also contain areas for cardiac medicine, since one of her greatest arguments was that one-fifth of all women who suffer heart-attacks have very different symptoms than men, such as back and side pain. But after hearing her pose this question more than thirty times, I wanted to scream. *Clearly* there is a department of the hospital that deals only with cardiac issues; in truth, the only specific and unique things a woman needs *are* mammograms and thorough pelvic exams. Personally, I have no qualms with the set-up of these apparently "unsophisticated" women centers. They efficiently cater to the feminine problems of the population and do not need to be slowed and interrupted by general medical problems.

Then there came the discussion of gender-specific medicine. Yes, I am all for this idea. If pharmaceutical companies were to formulate products that would better treat my medical problems as a woman, I would be immensely grateful. But Dr. Legato was bringing up ideas such as gender-specific toothpaste. We truly are an easily influenced society, one that is constantly looking to buy a quick fix and achieve a longer life span, and this avidity may be easily and unnecessarily exploited solely for financial gain. Maybe I'm wrong and separate toothpaste *would* be significantly beneficial, but I couldn't keep my eyes from rolling at this suggestion. I questioned Dr. Legato's motivation as soon as she prefaced her discussion with a description of the means by which she gained time and financial support for her project: by canvassing pharmaceutical companies, enticing them with thoughts of profit from future products.

Dr. Legato, on the other hand, claimed that her only inspiration came from the possibility of medical accomplishments and advancements that might ensue from her project's success. But in my opinion, her denied feminism and emotionalism fuel her mission as well. This is not necessarily a bad thing; she has committed no crime in incorporating her personal convictions into her work. But her adamant denial of doing so rather annoyed me. She constantly referred to her struggle as a woman researcher, alluding to her satisfaction upon receiving this grant after so much doubt and suspicion, as if it had finally shown male colleagues her importance and intelligence. She unfairly targeted males in the audience, presuming their egoism and ignorance regarding medical and social subjects related to the female sex. Feminism would have been an aspect of Dr. Legato's personality that I would have identified with and admired—once her quips started flying, however, this trait soon became obnoxious.

The weightiest issue she brought up was the literal black hole of information about pre-menopausal women, especially in my age range. She alluded to a cultural (and probably even global) phenomenon that prevents women from participating in research during that period of their life. Although women of all ages are quick to participate in observational studies that require no physical testing, almost no relatively young women participate in important clinical studies, most likely due to fertility issues. Men do not seem to have this problem and are quick to lend themselves to almost any medical research project. But women are much more hesitant about the conditions to which they will subject their bodies. One volunteer posed an interesting but completely unfeasible proposition: making it a national duty for women in certain age brackets to participate in clinical studies, kind of like signing up for the draft.

Basically what I took away was this: there are some pretty significant medical differences between men and women—but truthfully, there are important differences between any two individuals. Everyone reacts differently to disease and medications and splitting medical treatment between males and females could theoretically lead to separation of medical treatment for different races, ages, sexual orientations, etc. Essentially, everyone is unique and there is no universal protocol.

The application of some of the knowledge I have gained was performing an electrocardiogram, or an EKG. I was given a chart of positions for each electrode and literally felt my way through the situation. The woman to whom I was giving it was extremely cooperative and understood my inexperience. The test was not difficult to administer, but simple procedures like it are the closest I will come to actually "practicing" medicine at this point in my life.

Entry Five

I have had my first real bouts of uncertainty about my future in the medical profession. When I began working at the hospital, I wanted to get a comprehensive exposure to the experiences of a hospital doctor, whether good or bad. I never really considered the possibility of life-threatening circumstances, which, in retrospect, seems extremely imperceptive. Every patient who comes to the hospital has some medical ailment, so a hospital can almost be viewed as a Mecca of disease. Doctors place themselves in a hazardous environment every day, making themselves vulnerable simply because they have seriously committed themselves to that particular role in society.

A woman came in today, seeming to suffer solely from abnormally high blood pressure. After further investigation, however, this woman's medical history revealed seventeen operations and a general kind of degradation of body systems. When a patient needs blood drawn for testing, usually around six or seven tubes of blood are collected. The registered nurse was having a difficult time getting samples, mainly because most of the patient's veins had either collapsed or rolled over after so many surgeries. The nurse asked me to help, and I obliged (making sure she knew of my inexperience with such procedures). She handled the insertion of the needle, but instructed me on collection methods. Watching myself extract this "life substance" was a simple reminder of the amazing functions of the body. That this red liquid holds so much information about a person, that it is a unique, natural identification for every person, is—for lack of a better term—awesome.

So I had my safe, profound experience with blood. Unfortunately, a fellow hospital worker was not so lucky. After cleaning a room out, I noticed three doctors consulting seriously at the front desk. They asked for the extension of HIV/virology, and I automatically assumed an HIV patient had run into complications. The look on my face must have been a distinct mixture of incredulity and horror when I found out the person for whom they were calling HIV counselors was, in fact, a visiting medical student. Apparently he had been working in the ambulatory emergency room, observing an attending doctor deal with a new arrival. The patient was a homeless woman, suffering from generalized chest pain and shortness of breath. The attending had taken some blood samples and proceeded to hand them to the gloveless medical student. He reached over the patient instead of coming around to meet the student, and somehow punctured his thumb with the used needle. It was one of the worst states in which I had ever seen a person: a kind of frantic, internalized panic. The situation was gravely irrevocable and terrifying. The healthy, intelligent man may have contracted the HIV virus in just a split second—not by using intravenous drugs or practicing unsafe sex, but rather by simply doing his job. His life could be changed forever and shortened significantly, all because he chose medicine as his career. I wondered about the statistics and survival rates on such cases. Truthfully, I wished I didn't have to wonder about these mortality rates; I just kept watching the student search desperately for encouragement, asking every doctor he could find if they had ever been stuck. I saw the terrified look on his face while swallowing his first dose of HIV drugs and the anxious look in his eyes that scanned consent forms and paperwork with "HIV/AIDS" in bold print all over. Regardless of the fact that the disease was contracted completely accidentally and unfairly, he could still lead an extremely stigmatized future. I can say with certainty that HIV patients confront judgment and stereotypes everyday. I'm not proud to admit it, but I may have perhaps played my own part in the creation of this stigma, making sure I never touched their flesh without latex protection.

After the medical student left, a bizarre con-

versation ensued (at least in my mind). The nurses and doctors were talking about the situation, but strangely debating the severity of HIV versus that of Hepatitis C. I was floored. Most agreed that Hep C was a scarier prospect than HIV. I knew that Hep C was an autoimmune disorder that led to ultimate liver failure, but I didn't realize that there was a true lack of effective treatments. "At least you can aggressively treat the HIV virus," one nurse said. "Once your liver goes, you're done for." I guess I still have a lot of misconceptions to dispel.

Entry Six

In all of my shifts at the hospital, I have come to develop relationships with both doctors and patients. The ability to nurture true friendships with doctors is somewhat difficult in my department of emergency medicine, mainly because the longest period of time I've worked consistently with a doctor is one week. True, the relationships between patients and myself is even shorter, characterized as brief at best. But surprisingly, it is the personalities and interactions with patients that stick out in my mind and remind me of my time and purpose at Bellevue.

One patient I distinctly remember was a homeless woman, around thirty, who came in for abnormal abdominal pain. She was not alone, but accompanied by her two-month-old baby boy. After circumspect observation, the two appeared to be a normal, lower to middle class family. But after helping the patient with her examination and watching the baby during her periods of absence, I noticed subtle clues to the woman's life status. She had brought two bags to the hospital with her, probably containing all her possessions. I also noticed some common, identifying signs of homelessness in the woman, such as swollen, heavily veined legs and feet. But Bellevue sees many homeless people everyday. In fact, a majority of the patients are either unemployed, in shelters, or both. After a while, the situation becomes commonplace and homeless patients quickly assimilate with every other type of person to become, simply, homogenous patients. But what made this woman memorable to me were the signs of her absolute and complete devotion and love for her child. She was dressed in a soiled outfit, wearing dirty socks with holes. Her hair looked as if it hadn't been washed in a while, and she appeared rather pale. Her child, on the other hand, was clean and happy, clothed in crisp, blue overalls and immaculate white socks. He lay in a relatively new stroller, equipped with two prepared bottles of formula. She monitored him as if he were the most precious element in her constructed life. When I realized that my feelings of admiration were surfacing rather strongly, I took a few minutes to think about what exactly I had witnessed and responded to. It was a touching exposure to humanity, familial relationships, and almost tangible love—but it was also a kind of enlightened realization of the medical profession's purpose. Anyone involved in the field has the ability to attentively manage the well being of others on a daily basis, to truly spend their lives serving the most important element in *our* constructed society: people. And so I realized it wasn't so difficult to reaffirm my desire to join such a community of people; all I had to do was spend a few weeks in an emergency room, talking and listening to patients.

When Clean Becomes Too Clean

Sarah Hatoum

When it comes to cleanliness, it seems that to the typical American consumer, being dirt-free is no longer nearly enough. Rather, a widespread obsession with sterility has become popular. A simple trip to the local supermarket will illustrate this national obsession quite clearly. From kitchen cleaners to face washes, in order for an item to be seen as an adequate cleaning agent, it must be advertised as an antibacterial, an anti-allergen, a disinfecting solution, etcetera.

Yet as counterintuitive as it may seem, there is significant evidence, especially gained from animal testing, that an unusually clean environment may actually be harmful to one's health in the long run. An immune system that has been exposed to an unusually small amount of foreign substances will be relatively unprepared when it becomes exposed to a normal amount. This result seems to apply to humans as well. Children raised with pets, for ex-

ample, seem to experience less asthmatic wheezing than those raised with no pets[1].

Then there's the problem of bacteria. Antibiotic resistance is a story that's inspired fear both inside and outside the scientific community. It is a well documented and substantiated fact that bacteria exposed to antibacterial agents for a long enough period of time will grow resistant and are even capable of passing this resistance to other species. This makes bacteria progressively more difficult to kill and bacterial diseases much harder to cure. The fact that we are contributing to increased bacterial resistance as well as developing weaker immune systems through our excessive cleanliness may in fact create a medical crisis. Is feeling clean worth all the risks involved? When we consider the fact that many of the cleaning agents commonly used—such as antibacterial soap, for example—may not even be fulfilling the roles we expect them to—such as eliminating actual disease-causing agents—the answer becomes even clearer. True, antibacterial solutions kill harmful bacteria, but they do not kill the cold virus or the agents that cause several other minor illnesses. Since many of these illnesses are viral in nature, antibacterial soaps are useless in protecting us against them[2].

The companies producing such products must be aware of their limitations. Judging from their advertisements, however, they are not letting consumers know about them. Consumers should be informed of the potentially dangerous situation they face. While hygiene is an essential part of maintaining good health, our recent obsession with excessive cleanliness may in fact defeat its own purpose, leaving us in a medical crisis with which we are currently unable to deal.

References

[1] Litonjua, A. A. et. al. (2002) "A longitudinal analysis of wheezing in young children: the independent effects of early life exposure to house dust endotoxin, allergens, and pets" Journal of Allergy & Clinical Immunology. **110** (5): 736-42.

[1] Larson E.L. et. al. (2004) "Effect of antibacterial home cleaning and handwashing products on infectious disease symptoms: a randomized, double-blind trial" Annals of Internal Medicine **140** (5): 321-329.

In the News

States make plans to reimport prescription drugs from Canada despite federal opposition

Seeking relief from the high cost of prescription drugs, a number of states and local communities have made plans to re-import US manufactured drugs from Canada, where drug costs are significantly lower because of government price controls. Altogether, twenty-four state governments have considered plans to re-import drugs from Canada in some form, including Minnesota, New Hampshire, Iowa, Illinois, West Virginia, Wisconsin, and even Boston Mayor Tom Menino.

Federal law, however, allows re-importation only if the secretary of Health and Human Services (HHS) certifies that the practice is safe—something that HHS Secretary Tommy Thompson has refused to do. "The law requires me to certify [prescription] drugs coming from another country are safe. That is a hurdle I can't meet," he said. In fact, the Food and Drug Administration (FDA) has begun to threaten legal action against states that plan to implement a re-importation program. FDA officials recently wrote to Minnesota Governor Tim Pawlenty (R), calling the state website that connects residents with Canadian pharmacies "unsafe, unsound, and ill-considered." According to FDA Associate Commissioner William Hubbard, "the law is very clear. It's undeniably illegal to import unapproved foreign drugs…There's no question about that."

Senator Edward Kennedy (D, MA), however, echoed the sentiment of many Democrats and some Republicans when he said, "This is not about the safety of prescription drugs…[Rather,] the administration is worried about the profits of the pharmaceutical industry." In response to FDA safety concerns, Pawlenty said, "Show me the dead Canadians. Where are the dead Canadians?"Last July, the House of Representatives approved a bill on a 243/186 vote that would have legalized the re-importation of prescription drugs (HR 1). Rather, it continued to permit prescription drug re-imports, but only upon certification by the HHS secretary. The bill also established a commission to study how to re-import drugs safely.

TuftScope
Mayer Campus Center
Tufts University
Medford - Massachusetts - 02155