

HEALTH ADVOCACY BULLETIN

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BARTH SYNDROME

Responding to a Genetic Disorder: A Case Becomes a Cause

By *Katherine R. McCurdy*

It was a Saturday in April 1988 and my mother-in-law's 70th birthday. Unbeknownst to her, the entire family was arriving from around the country to celebrate. Our only hitch was minor, we thought: our two-year-old son had a cold and had awakened early, crying and uncomfortable. When we picked him up, he seemed OK (except for some congestion), but my husband and I immediately noticed that his chest was heaving visibly with every rapid heartbeat. As morning broke, I called the pediatrician to ask if he could squeeze us in, which he graciously did. Upon exami-

nation, the doctor agreed that my son, Will, did not seem in distress; he was concerned, however, that Will might have an infection that would require intravenous antibiotics. He instructed me to go to our regional tertiary care hospital's Emergency Room where the Chief of Pediatric Cardiology, whom he had already alerted, would meet us. As he spoke, I heard the first of many medical terms that were completely new to me that day—"tachycardia." We were already aware of some mysterious gross motor problems that our son had exhibited, but we had taken him to many of the best medical centers up and down the East Coast, and none of the top-notch

specialists had been able to make a diagnosis. Anything cardiac was new. I remember wondering in the ER whether all this might lead to something bigger and broader. Little did I know that we were embarking on the journey of a lifetime.

The cardiologist, whom we soon came to revere for his knowledge and sensitivity, told us that Will was very sick and might need a heart transplant. Will was admitted to the Pediatric Intensive Care Unit. Four hours earlier, we had thought we were dealing with a cold! We were suddenly thrust into a world about which we knew almost nothing...and the life of our child was at stake. Fortunately, we were in excellent hands. Unfortunately, we were going to discover that even the best physicians had few satisfying answers.

Numerous specialists were summoned to analyze Will's array of medical problems. It was determined that he suffered from neutropenia (periods during which one type of white blood cell would vanish, leaving him dangerously susceptible to infection) in addition to cardiomyopathy and skeletal muscle weakness. A computer search for any disorder that shared these three primary manifestations yielded a single paper written by a Dutch neurologist named Peter Barth. This article described an X-linked recessive genetic condition that had ravaged one Dutch family and sounded very much like what Will had. But we had no hint of this in our family tree.

The gene for this syndrome had not yet been identified, and there was no marker test available. The geneticist with whom we were working wrote to Dr. Barth seeking his advice about the diagnosis and inquiring about treatments that

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From the Editors

When Marsha Hurst, Director of the Health Advocacy Program (HAP), and Caroline Lieber, her counterpart in the Human Genetics Program (HGP), called for student volunteers to serve as editors for this issue of the *Health Advocacy Bulletin*, we jumped at the opportunity. The *Bulletin* is the journal of the HAP at Sarah Lawrence College, and this issue marks the first edition jointly published by the HAP and the HGP.

The cracking of the code for the human genome is an earthshaking event. Although scientists have barely begun unraveling the function of an estimated 35,000 genes, along with their protein products, it is clear that a new biological paradigm has already taken hold among both scientists and the general public. In

creating this new biological paradigm, it is crucial that all affected parties have a seat at the table.

We like to believe we are far beyond the era of Edward Jenner who, drawing upon folklore that milkmaids exposed to the mild disease cowpox were immune from smallpox, injected several children with pus from cowpox pustules. The criticisms of his contemporaries were misplaced in that they ignored the impropriety of using these children as guinea pigs. Fortunately, his efforts were successful and his theory proved valid. Sadly, however, the tendency to trust scientists and medical practitioners to "first, do no harm," has too often allowed horrendous outcomes, viz., the Tuskegee study or the sterilization of women on welfare. In this issue, Rachel Grob out-

lines some social and ethical issues that are addressed in helping create this new biological paradigm for SLC students enrolled in both the advocacy and genetics programs. Meg Howard attests to the value of these joint studies in her article attempting to bridge the two disciplines.

It is at the nexus of concerns of geneticists and advocates that we have tried to position this special *Bulletin*. The articles by Alice Herb and Kathi Hanna discuss specific areas in which medical, ethical and moral issues collide, as well as subsequent attempts to reconcile this welter of competing agendas. Unfortunately, when governments participate in these attempts, they often assume moral mandates well beyond their electoral majorities (e.g., stem cell research). On the other hand, majority opinion does not necessarily align with truth. See Pat Banta's historical perspective on U.S. government attempts to engage in the creation of this emerging biological paradigm.

Ever at the vanguard of knowledge, scientists consistently push the envelope, and advocates, striving to protect the innocent, used and abused, push an oftentimes competing envelope. An advocate's awakening is poignantly related by Katherine McCurdy in her piece about Barth syndrome. And two articles about autism are presented as a point-counterpoint, illustrative of the tension at the nexus of genetics and advocacy—a necessary, but hopefully creative, tension.

With the advent of the internet, information has become infinitely more accessible, but as a double-edged sword; misinformation is also readily at hand. Genetic information is much desired by patients, their caregivers and relatives, and Paige Hankins helps readers sort out the good from the bad in her guide to using this new vehicle effectively. Peter Thom and Sharmila Padukone take geneticists to task for their importation of socially constructed racial terminology, which, in genetic terms, is misleading and imprecise. Finally, Erin Carter reports on a visit to Sarah Lawrence by Diane Paul, author of several books on eugenics, evolution and the politics of heredity.

Inevitably, the fields of genetics and advocacy have become inextricably intertwined. In this issue, we have tried to draw on the expertise of those in both disciplines to reflect ways in which joint efforts are contributing to the development of a genetic citizenship.

—Peter Thom and
Sharmila Padukone

INTRODUCING OUR GUEST EDITORS...

Two Human Genetics Program students, Peter Thom and Sharmila Padukone, have worked hard as both editors and authors to help create this special issue. We thank them and take great pleasure in introducing them to our readership.

Born in Edinburgh, Scotland, Peter came to the U.S. by way of Montreal. After a successful career as a singer, songwriter and composer, he decided to embark upon a new challenge. His long-standing interest in genetics, fueled by discussions with his brother-in-law about his work with the genome project, led to Peter's decision to enter the HGP last year. He is most grateful that his wife and daughters are enthusiastic supporters of this metamorphosis.



Peter Thom



Sharmila Padukone

Sharmila's interest in genetics began in India, where she received an undergraduate degree in zoology and a masters in cytology and genetics. Starting with a research fellowship, she worked in cancer endocrinology, pharmacogenetics and population genetics before coming to the United States in 1999. Sharmila is also an interior designer, a photographer and an Indian classical dancer. She appreciates the support of her family, especially her daughter Anvita, who has been staying in India so that Sharmila could concentrate on her studies.

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Autism, a controversial topic involving genetics and advocacy, has received recent attention in the scientific and popular media. Following are an article on the subject written by two HGP students, a response from an autism advocate and a reply to the response. Readers are invited to contribute to the discussion by submitting their personal views, which we will share in future issues.

Autism: Piecing the Puzzle—Together

By Peter Thom and Shifra Krinshpun

The headline in *The New York Times* March 4, 2004 leapt out: "Researchers Retract a Study Linking Autism to Vaccination." For several years, a fierce controversy has been simmering; on the one hand are those who claim a link between autism and early childhood measles, mumps and rubella vaccinations (MMR) and, on the other, those who assert that no such link has ever been proved.

The retracted study was originally published in February of 1998 in *The Lancet* (Wakefield et al., 1998). Twelve children with chronic enterocolitis and regressive developmental disorder were studied. The authors stated clearly in their discussion section: "We did not prove an association between measles, mumps, and rubella vaccine and the syndrome described." At the press conference when the study was released, however, the lead author suggested that an association might well exist, and that parents might wish to consider single vaccinations for measles, mumps and rubella, rather than the combined shot. This suggestion apparently found a wide audience. As Mayer (2004) discovered five years later, in Britain, the autism/MMR link had gained such wide credence that MMR vaccination rates had fallen by more than 10% to 82% (95% is the goal for control or eradication of most diseases).

Unfortunately, during that five-year period the frequency of measles outbreaks in Britain increased as well, with consequences unknown. For historical purposes it is useful to note that, according to the U. K. National Health Service, prior to widespread MMR immunization, 500,000 children contracted measles each year, resulting in 100 deaths. After 1968, as the vaccination uptake slowly increased, infections gradually decreased. There have been no acute measles deaths reported in the United Kingdom since 1992 (National Health Service, U. K.). As recently as 1999, there were nearly 870,000 deaths worldwide

from measles, mostly in countries that had not implemented vaccination programs (World Health Organization, 2004). Indisputably, vaccination has saved lives.

Since that *Lancet* study was published in 1998, there have been many studies refuting the autism/MMR connection. For example, in 2001, a study in *The Journal of the American Medical Association* found that, although autism cases in California increased by 373% between 1980 and 1994, MMR uptake during that period increased only by 14% (Dales, Hammer & Smith, 2001). And, in a systematic review of current epidemiological evidence, the results of 12 major studies examined showed that "The current literature does not suggest an association between ASD [autism spectrum disorder] and the MMR vaccine; however, limited epidemiological evidence exists to rule out a link between a rare variant form of ASD and the MMR vaccine." Their concluding recommendation was, "Given the real risks of not vaccinating and that the risks and existence of variant ASD remain theoretical, current policies should continue to advocate the use of the MMR vaccine" (Wilson, Mills, Ross, McGowan & Jadad, 2003).

The theory that vaccines are linked to autism gained adherents in the United States after thimerosal was identified as a viable cause, worthy of investigation. Thimerosal, a mercury-containing compound, is a known neurotoxin and has long been used in certain vaccines to prevent microbial contamination. However, thimerosal cannot be used in MMR because MMR is a live vaccine and thimerosal would kill the vaccine's inactive viruses used to prod the immune system into generating protective antibodies. The thimerosal controversy rages on, though, because of its use in other childhood vaccines (e.g., DPT). There are several papers describing large studies that have shown no causal link between thimerosal and autism (Verstraeten et al., 2003; Reading, 2004; IOM, 2004). On May 17, 2004, an Institute of Medicine (IOM) press report summarized their findings

to date: "The committee concludes that the body of epidemiological evidence favors rejection of a causal relationship between the MMR vaccine and autism."

Fortunately, the fourth estate thrives not only on hyping controversy but also on uncovering scandal. The *New York Times* story cited earlier would perhaps never have been written, and the debunking of the connection of MMR vaccines to autism never widely disseminated, but for a scandal involving the lead author of the study (Wakefield et al., 1998). He had apparently earned over \$100,000 as an expert witness in a legal case involving some of the children in the original study—a clear conflict of interest that he never declared. When this came to light, *The Lancet's* editors, along with most of the article's authors, were duly embarrassed, leading to the retraction of the article.

Changing Clinical Criteria

The Centers for Disease Control and Prevention (2004) summarizes the results of several studies indicating that the incidence of autism ranges from 3.4–6.7/1000 children. Autism can be devastating for both the affected children and their parents. Between 40% and 70% of autistic children have mental retardation; about 25% have epilepsy (Aurenan, 2002). A recent study of autistic adults by Howlin, Goode, Hutton & Rutter (2004) found that "within the normal IQ range outcome was very variable and, on an individual level, neither verbal nor performance IQ proved to be consistent prognostic indicators. Although outcome for adults with autism has improved over recent years, many remain highly dependent on others for support."

Why has the prevalence of autism increased so dramatically? According to some medical researchers, the preponderance of evidence shows that clusters of higher incidence of autism in New Jersey and California are more likely to reflect the application of recently broadened diagnostic criteria and greater awareness on the part of both parents

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and professionals rather than any environmental contamination or causative environmental factors that are particularly concentrated in those specific regions (Jick & Kaye, 2003; Coury & Nash, 2003). Likewise, the drastic increase in prevalence estimates of autism from 2-5 in 10,000 to more than 1 in 1,000 is also likely to have been the product of the revised diagnostic definitions (Folstein & Rosen-Sheidley, 2001), enumerated by the ICD-10 (World Health Organization, 1993) and the DSM-IV (APA, 1994). Environmentalists counter these studies by insisting that clusters are difficult to verify using standards of knowledge based on epidemiological methodology because of the small size of most clusters. They assert that cluster studies are consistently undervalued by mainstream medical researchers, who use a methodological approach inherently biased against environmental impact on small populations (Steingraber, 1998).

The broadening of the diagnostic criteria did not occur suddenly but developed gradually, undergoing several revisions to accommodate the findings of research that examined and evaluated the autistic phenotype. From these changes in diagnosis, many patients previously unlabeled are now deemed autistic. The California Department of Developmental Services (2003) reported that an analysis of statewide data from 1987 to 2002 showed that “The greatest yearly proportional changes were reductions in the percent of persons with autism and a coexisting diagnosis of Moderate, Severe or Profound MR and the corresponding increase in the percent of persons with [autism and] no mental retardation.” Logically, if vaccinations caused this overall increase in autism, there should have been a proportional increase across the spectrum. Yet, the increase was restricted to those with no concomitant mental retardation.

Nevertheless, the question remains: is the increased incidence in autism “real,” i.e., not attributable to better ascertainment of hitherto undiagnosed but affected people? As Lisa A. Croen and Judith K. Grether (2003) have stated, “Unfortunately, we currently lack the data to evaluate secular changes in autism incidence. By using a standardized case definition and multiple-source case ascertainment strategy over time in a

well-defined population, the true rate of occurrence of autism can be evaluated.” This is an important question because the case for an environmental insult as the cause for the observed increased incidence of autism rests largely on the assumption that the preponderance of this increase is real.

The first clinical description of autism was presented in 1943 by Leo Kanner, an American child psychologist, who characterized 11 children, mostly boys, as having tendencies to withdraw socially and isolate themselves, behaviors that precluded social interaction. He called this unique behavior *infantile autism*, reflecting its early onset. Kanner formulated the condition appropriating Eugen Bleuler’s term autism, coined in 1916 as a behavioral description of schizophrenics, who also often withdraw from public settings. The historical association between Bleuler’s autism and schizophrenia influenced the classification system presented in the second edition of DSM (APA, 1968), which included autistic disorders under the diagnostic criteria of childhood schizophrenia (Auranen).

Based on the early presentations of autism, Kanner had hypothesized that there may be an underlying genetic or neuropathological component responsible for the behavioral patterns seen. However, his later suggestion that the autistic phenotype is precipitated by parents’ cold, inattentive attitudes toward the child gained more notoriety than the scientific-based explanation. The psychiatric community’s endorsement of parenting deficiencies as the cause of autism followed, and was influenced by several factors. First, there was speculation that the lack of dysmorphic features normally associated with cognitively impaired children contradicted the idea that autism was an inborn disorder. Second, the observation that the parents tended to be socially reticent bolstered the concept that the child’s autistic behavior was learned. Finally, the psychiatric model that prevailed during the 1950’s pinned everything on deficient parents and early upbringing. Cold mothers, so-called “refrigerator mothers,” were seen as the cause of the socially-isolated phenotype seen in autism (Folstein & Rosen-Sheidley; Rutter, 2000).

In the third edition of DSM (1980), after the hypotheses and works of Bernard Rimland, Susan Folstein, Michael Rutter

and Lorna Wing had been recognized, autism emerged as a separate and distinct syndrome. In 1964, Rimland proposed the neural theory of behavior, which challenged the assumed causality of bad parenting. In 1977, Folstein’s and Rutter’s autism twin study demonstrated greater concordance between MZ (monozygotic) twins than DZ (dizygotic) twins, establishing a strong genetic basis for autism. In other words, while the risk that both fraternal twins will be affected with autism is $\approx 3\text{-}7\%$, the comparable risk for identical twins is $\approx 60\%$ (Stodgell, 2000). Because identical twins share an exact complement of genes while fraternal twins share only half, geneticists have definitively concluded that heredity plays a significant role in autism.

Lorna Wing, in 1979, identified the triad of abnormalities found in varying degrees of severity among affected individuals: socialization, social communication and social play (Auranen). This triad of abnormalities was used in the classification system by the DSM-III in delineating diagnostic criteria for a group of autistic-like disorders, collectively known as pervasive developmental disorders (PDD). In the revised version, DSM-III-R, the criteria expanded to include yet another subgroup named pervasive developmental disorder not otherwise specified (PDD-NOS), which included Asperger syndrome (AS).

Wing (1997) further expanded the existing diagnostic criteria by including cases of mild mental retardation, abnormal development in verbal and communication skills, and female cases. The DSM-IV, published in 1994, reflected Wing’s modified criteria and included AS. The ICD-10 also redefined its PDD category, adopting the new diagnostic definitions (Auranen).

The current PDD spectrum has broadened still further to include Rett syndrome and Childhood Disintegrative Disorder (CDD). Rett syndrome is an X-linked genetic disease characterized by progressive neurological degeneration, marked by rapid deterioration of psychomotor skills and subsequent stabilization. This disorder is almost exclusively seen in females, so it is speculated that the disease is lethal among males in the prenatal/neonatal period. Recently, a gene has been found to be the cause of Rett syndrome (Amir et al., 1999).

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Advocacy: Responsible— and Irresponsible

Parents of autistic children crave reliable information that might put their lives into perspective. They become stressed over how difficult it is—will always be—to care for these children. They agonize about who will care for the child after they have gone (autistic patients appear to have a normal life span). Media dissemination of faulty science, as exemplified by the retracted study (Wakefield, 1998), has helped persuade many parents that vaccinations were to blame for their children’s autism.

But the media, unfortunately, are not alone; advocacy groups must share part of the blame. In researching this paper, we were struck by what Christopher Trevors, a recent HGP graduate, reported in his thesis (Trevors, 2003). The thesis proposal was to interview parents of autistic children to elucidate the psychosocial issues of daily life for their families and educate genetic counselors dealing with such families. He describes

the difficulty recruiting families: “I contacted the organizer of the local chapter of the Autism Society of America (ASA). At first she was very excited by the idea behind my project and was eager to help me obtain other families to participate. This enthusiasm lasted until she discovered that I was a genetic counseling student. She immediately responded with, ‘This isn’t our fault; we didn’t give this to our children.’” Trevors also describes the guilt, defensiveness and unresponsiveness he found among parents of autistic children.

While writing this article (April to June, 2004), we visited the website for the ASA on several occasions. During this period we could not find there any links highlighting the recent retraction by *The Lancet* of the article by Wakefield et al. (referenced earlier in *The New York Times*). On the website, the link “Theories on the Causes of Autism” led us to this: “In a 2001 investigation by the Institute of Medicine (IOM), a committee concluded that the ‘evidence favors rejection of a causal relationship... between MMR vaccines and autistic spectrum

disorders (ASD).’ The committee acknowledged, however, that ‘they could not rule out’ the possibility that the MMR vaccine could contribute to ASD in a small number of children. While other researchers agree the data do not support a link between the MMR and autism, more research is clearly needed.” Fair enough, given the state of knowledge in 2001. But, as noted above, there is much in the way of new evidence in the last three years.

One of the principal presenters at the most recent meeting of the IOM (February 9, 2004) was Kumanan Wilson, who, in his 2003 study of epidemiological evidence concerning the MMR/autism link, concluded that the *real* risks of not vaccinating outweighed the *theoretical* risk of the MMR/autism link. Initially (April, 2004), we could not find mention of this study, or its conclusions, anywhere on the ASA’s website. By contrast, several other presentations at the same conference were noted—those highlighting the purported link between thimerosal and

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Pervasive Developmental Disorders *

PDD Disorder	Clinical Characteristics/ Age of Diagnosis	References
Infantile Autism	Delayed onset or regression of speech which can be associated with other cognitive deficits; frequent failure to develop attachment to their caregivers as well as minimal interest in their age-related peers; tendency to express rigid and repetitive (<i>R & R</i>) behaviors, including hand flapping, and preoccupation or intense focus on specific interests; frequent deficits in social aspects of communication (pragmatics) such as the inability to display interest in the thoughts of others, to maintain eye contact, and to know when to stop talking; frequent demonstration of echolalia. Signs are present at birth, with <i>R & R</i> appearing at 36 months. Diagnosis usually occurs during second to third year of life.	Folstein, S.E. & Rosen-Sheidley, B., 2001; Wing, L., 1997; DMS-IV (APA) ICD-10
Asperger Syndrome	Typically not associated with cognitive defects; motor clumsiness is frequently observed; normal language development; repetitive speech may be observed; frequent inability to empathize and interact socially; commonly considered as loners; highly functional.	Miles, J.H. & McCathren, R.B., 2003; Auranen, M., 2002
Rett Syndrome	Display normal psychomotor development until six to eight months with regression in language and motor skills thereafter; neurological degeneration associated with severe cognitive impairment; characteristic hand-wringing movements, body-rocking; socially withdrawn; 50% have seizures; development of hand and foot deformities are common; majority of cases are females; prevalence 1/10,000 – 1/15,000; usually diagnosed between two and five years of life.	Zoghbi, H.Y., 2004; Department of Developmental Services, California, 1999
PDD-NOS	Some autistic features are present, however they do not meet the full criteria for autism; deficits in communication and social interaction are generally milder than a typical autism case. Individuals usually have higher functioning and typically respond to treatment.	Department of Developmental Services, California, 1999
CDD	Development is normal for two or more years before showing loss of nonverbal communication, language and social skills, as well as motor skills and other acquired functional skills. Least common diagnosis/prevalence of PDD disorders.	Department of Developmental Services, California, 1999; Miles, J.H. & McCathren, R.B., 2003

* Not all forms are included.

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autism. On the home page, and highly visible, there was a link to a study describing mechanisms whereby thimerosal may adversely affect neurodevelopment (Waly, 2004).

In May, the ASA website did report on the conclusions of the IOM press release of May 17, 2004, which found no causal relationship between MMR and autism, or thimerosal and autism. Dr. Tom Saari, a professor of pediatrics at the University of Wisconsin Medical School in Madison and a member of the American Academy of Pediatrics (AAP) committee on infectious diseases, described that report as “awful darn close to the final word” (Gardner, 2004). However, the ASA (May 2004) rejects the study’s conclusions stating: “Those in the autism community who believe there is a link argue that vaccines only affect a small portion of the total population with autism—those who are genetically predisposed—and thus large-scale, epidemiological studies, which do not prove cause and effect, cannot appropriately answer the question at hand.” The president of the ASA further elucidated its position, saying, “Right now, we have two hypotheses in juxtaposition to one another. No matter which one is proved or disproved, until we study the actual population allegedly affected, we will not have a resolution to this personal and human tragedy.”

It can be plausibly argued that large-scale epidemiological studies may not pick up an environmental/genetic link to autism among a small subset of individuals with autism. For this reason, we consider the case for a thimerosal link to autism not yet definitively disproved, though the preponderance of evidence to date weighs against such a causal link. The IOM study released in May 2004 noted that “...the body of epidemiological evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism. The committee further finds that potential biological mechanisms for vaccine-induced autism that have been generated to date are theoretical only.”

From “Refrigerator Moms” to Candidate Genes

By the mid to late 1960’s, there was some evidence implicating neurobiology and genetics in autism. By 1977, the first

epidemiological twin study produced very high heritability estimates for autism (Folstein & Rutter), suggesting significant genetic causes. This was even more striking when a broader phenotype, including milder social and cognitive deficits, was examined. Identical twins, originally judged not to share symptoms of autism under narrower diagnostic criteria, more frequently did share milder forms of social reticence and language disabilities. Siblings and parents of autistic children also tended to be more socially reticent and have more communication deficiencies and difficulties with changes in routines than controls (Eisenberg, 1957; Steffenberg, 1989; Bailey, 1995).

One of the unexplained peculiarities of autism is the sex ratio of affected children. Overall, it is reported as being about 4:1, male:female. However, this ratio is even higher in the milder phenotype. The currently accepted genetic model for autism posits anywhere from two to ten interacting gene loci (epistatic gene loci theory)—most likely three to six genes. The variation in severity of symptoms between individuals is explained by this model as being dependent upon the number and the specific mix of interacting genes a child inherits (Pickles, 2000).

An alternate theory involves the immune system. There appears to be more autoimmune disease in families of autistic children than in controls without autism (Comi, 1999). This is a class of disorders in which the body’s defenses cannot distinguish “self” from “other” and attack the body’s own tissue; e.g., multiple sclerosis, rheumatoid arthritis and early onset diabetes. The theory is that there may be an inherent susceptibility for autism in some people that is triggered by environmental and/or immunogenetic risk factors. In June 2004, M. Hornig, D. Chian and W. I. Lipkin reported a study on the link between environmental and immunogenetic factors. Their conclusions, released on the heels of the May 2004 IOM study, supplied additional fuel to the raging controversy over the use of thimerosal in vaccines. The authors found that mice with inbred immune deficiencies developed autism-like symptoms when exposed to quantities of thimerosal proportionate to those received by human children. Without doubt, this study should prompt further investigation. However,

we would urge some caution: precise extrapolation of biochemical effects from the mouse model to humans is not always valid. Moreover, autism diagnoses are difficult enough in humans, let alone in mice. And the study makes the speculative assumption that autism is the consequence of an autoimmune reaction.

Whichever theory turns out to be correct, it is likely to be better elucidated through genome screens of families with autism. A number of these have been completed and more are currently under way. The data thus far are confusing, pointing to many candidate genes, consistent with the epistatic loci theory described above. Moreover, there is very little overlap of candidate genes from one study to another. One alternate approach has been to examine genes in regions of a chromosome linked to autistic families, in particular, genes that play a role in fetal brain development. Another is to study potential genetic differences between MZ twins who are discordant. In other words, in cases where identical twins do not share autistic symptoms, close study of each twin may tease out some answers, whether they are genetic or environmental. Genetic explanations for autism, as for many so-called multifactorial diseases, are likely to be quite complex, involving inherent susceptibilities as well as possible environmental triggers. Interpreting them for the lay public will require both geneticists and advocates to become familiar with a plethora of complex, rapidly-changing and often contradictory research results.

Some Final Observations

The peer review process must efficiently screen out poorly designed studies, thereby preventing widespread dissemination of studies of dubious merit. The retracted study in *The Lancet*, highlighted earlier, has been criticized by many, including Professor Trisha Greenhalgh, an expert on evaluating scientific studies and the author of *How to Read a Paper—the basics of evidence-based medicine*. She concludes her evaluation with a scathing indictment: “In conclusion, the Wakefield study was scientifically flawed on numerous counts. I am surprised that neither the editor nor the reviewers spotted these flaws when the paper was submitted. Had they done so, the public would have been saved the confusion and anxiety caused by false

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credibility conveyed by publication of the study in this prestigious journal” (Greenhalgh, 2004).

Although the purported links between autism and both thimerosal-containing vaccines and MMR vaccines have now been found to be tenuous, much of the public still believes the claims. One of the authors of this article, who has a relative with autism, recently reported to the boy’s mother about the numerous studies presenting evidence against the autism/vaccine linkage. The mother responded that she had thought it was proven and seemed disturbed to

hear that the preponderance of evidence refutes such a link. It was as if the purported vaccine link had been a receptacle into which blame for her child’s affliction had safely been placed.

Some assert that no harm has been done; that if the goal has been to assuage those who must live with the daily trials of autism and that goal has been accomplished, then even false constructs suffice as balm. But, as scientists, we should refrain from ends-justify-means argumentation. In our opinion, geneticists and advocates should move to correct theoretical constructs whenever the preponderance of available evidence contradicts those current beliefs. For the sake

of all those who struggle daily with the consequences of caring for family members with autism, it is our hope that together, geneticists and health advocates can begin to undo whatever harm flawed science has wrought to diagnostics, research strategies, management, parental counseling protocols and efficient use of advocacy resources.

Shifra Krinshpun studied cellular biology, genetics and art history at Brandeis University. She is currently working toward her master’s degree in the HGP. Guest editor/author Peter Thom is introduced on page 2.

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Vaccine Safety and Autism: The System Is “Broke,” Let’s Fix It

By Sallie Bernard

Childhood vaccines save lives from infectious diseases, but, like any other potent medical product, they can have side effects. Since vaccines are given to virtually every infant worldwide, diligent characterization of side effects and their elimination must be a public health priority. Unfortunately, our public health officials and vaccine manufacturers spend far more effort and resources on promoting new vaccines and higher vaccination rates than they do on safety, to deleterious effect. The MMR vaccine and the mercury-based vaccine preservative thimerosal, both recently linked to autism, provide painful but illustrative examples of safety lapses on the part of health officials and manufacturers. The inadequate response by these parties to safety concerns over MMR and thimerosal has led parents to question immunization programs.¹ Until vaccine safety oversight is handled properly, public confidence in vaccination will continue to erode.

Autism is a severe neurodevelopmental disorder with onset in early childhood. It was once thought to be rare, affecting one in 5,000 children, and to be caused by genetic mutations.² It is only in the last few years that a connection has been widely made between autism and vaccines. There are a number of reasons for this development.

The prevalence of autism reported in epidemiology studies has steadily increased over the past 20 years. In the 1990’s, the rate skyrocketed. The Centers for Disease Control and Prevention (CDC) now gives an official incidence of autism spectrum disorder among children of one in 166. While some researchers argue that the increase is due to better awareness of the disorder and changing diagnostic criteria,^{3,4} others have refuted this hypothesis, saying the increase is real. For example, the respected epidemiologist Robert Byrd, in analyzing the California developmental disabilities data set, declared the increase in autism to be real and not due to such factors as

immigration into the state or changes in diagnosis.⁵ A paper by Croen et al. suggesting that the increase was due to shifting of diagnoses away from mental retardation and into autism³ was soundly refuted by Spitzer and colleagues,⁶ a criticism to which Croen et al. acceded.⁷ As Mark Blaxill points out in an upcoming exhaustive review,⁸ the diagnostic criteria have not changed enough to result in meaningful differences in inclusion/exclusion rates, and, if the incidence of autism has always been 1 in 166, why has no one been able to identify the “hidden hordes” of autistic adults who must exist in group homes and institutions? He points to a study in the Midwestern U.S., which failed to find any adult “hidden hordes.”⁹ In recognition of the weakness of research refuting an increase in incidence, the director of the CDC, Dr. Julie Gerberding, stated in a 2004 meeting with autism advocates that the weight of the evidence supports a true increase in the rate of autism.

If autism is truly on the rise, then an environmental agent must be involved in its etiology. Genetics alone cannot explain an abrupt change in disease prevalence. A gene-environment interaction makes intuitive sense. As Dr. Kenneth Olden, Director of the National Institute of Environmental Health Sciences of the NIH explains, very few diseases are either purely genetic or purely environmental; rather, the vast majority arises from a genetic susceptibility triggered by an environmental insult.

If an environmental agent is involved in autism etiology, what would be the most likely candidates? The live virus measles vaccine and thimerosal are logical choices for a number of reasons. Viruses are known to cause autism and autistic-like symptoms under certain conditions.¹⁰⁻¹⁴ Mercury is also known to cause symptoms and abnormalities found in autism.¹⁵⁻¹⁹ Parents report normally developing children who regress into autism after vaccination, providing evidence of a temporal association which is a necessary component in establishing causality. On an ecological level, the

rise in autism prevalence has corresponded with the effort of public health officials worldwide to improve on-time and complete compliance with national vaccination schedules beginning in the late 1980’s, and with the introduction of two new thimerosal vaccines in the 1990’s, the Hepatitis B and the *Haemophilus Influenzae* type B.²⁰

The biological evidence for an MMR and thimerosal link to autism is compelling and growing. Several studies have replicated the original findings of Andrew Wakefield that a subset of autistic children suffer from bowel disease and that measles virus is present in biological samples taken from autistic but not control children.²¹⁻²⁵ Measles virus has been detected in both the intestinal tract and in the cerebrospinal fluid. While it is not proven that the measles are causing the autism, given that measles, through the SSPE (subacute sclerosing panencephalitis) disease, is capable of producing neurological symptoms, it seems prudent to determine whether this is happening in autism.

Biological evidence to date supports an association between mercury exposure and autism. A case-control study investigating mercury levels in baby hair of children later diagnosed with autism found less mercury despite equal or higher exposures than the control group, raising the possibility of impaired excretion capacity for mercury in autistic children.²⁶ This finding was replicated by investigators at MIT.²⁷ Another study measured mercury in urine after administration of a chelating agent among autistic versus normal children. The autistic children excreted more mercury with the intervention, suggesting a higher mercury body burden in the patient group.²⁸ Several research labs are finding alterations in the methionine transsulfuration pathway in autistic children, which can lead to lower glutathione levels.^{29,30} Glutathione is a primary mechanism which the body uses to counteract the harmful effects of mercury due to oxidative stress. In fact, there is mounting evidence that autistic chil-

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dren suffer from increased oxidative stress, which can lead to neurological and immune damage.³¹ Mercury, including thimerosal, is a potent inducer of oxidative stress.³²

Research on the toxicity to cells of even small amounts of thimerosal, like those found in vaccine doses, is now emerging in the literature. At such levels, thimerosal can cause cell death through apoptosis and inhibit key enzymes necessary for normal development.^{30,33} Results are showing greater immunotoxicity from thimerosal than methylmercury,³⁴ and equal neurological toxicity to methylmercury.³⁵ A study on mice prone to autoimmunity was recently completed by researchers at Columbia University.¹⁵ They dosed infant mice with vaccines containing thimerosal, following a vaccine schedule similar to the CDC-recommended program, adjusted for mouse developmental age and weight. The mice developed brain lesions in hippocampus and Purkinje cells, macrocephaly from white matter enlargement, learning difficulties, reduced exploratory behavior and other abnormalities characteristic of autism in humans. An NIH-funded study among primates³⁶ compared brain and blood levels after equal doses of mercury from thimerosal and methylmercury. While blood levels were lower for the thimerosal group, the brain: blood ratio was proportionately higher relative to the methylmercury group. Long-term mercury accumulation in the brain was twice that for thimerosal, due to its far more rapid conversion to inorganic mercury, a lipophilic form which takes years to leave the central nervous system.³⁷

In fact, the findings from the NIH primate study leave in doubt the conclusions of a human study used by public health officials to refute claims of harm from thimerosal. This study,³⁸ led by an immunologist with extensive involvement in vaccine development, measured blood mercury levels in infants after vaccination and found the levels to be lower than those expected from methylmercury exposure. They inferred that, because blood levels were lower, the chance of harm was minimal. Yet this group did not measure long-term mercury levels in the brain, as the primate study did. The primate study demonstrates that lower blood levels from

thimerosal can mean higher long-term mercury levels in the brain.

The response from public health officials to the growing biological evidence has been to counteract it using epidemiology studies. These studies, unfortunately, have mostly been conducted by CDC insiders or employees of vaccine manufacturers and suffer from major methodological deficiencies. Moreover, the data sets relied on for a number of these studies have been deliberately closed to other researchers, making replication of the findings impossible.

As Dr. Jeff Bradstreet explained in a paper presented to the Vaccine Safety Review Committee of the Institute of Medicine (IOM),³⁹ “Epidemiological studies that have examined the possible MMR-autism association have concluded that the data provide no evidence in support of this hypothesis.⁴⁰⁻⁴⁴ These studies have been challenged on a number of counts including inappropriate methodology,⁴⁵ lack of statistical power and lack of a control group,⁴⁶⁻⁴⁷ indiscriminate diagnostic groupings,⁴⁸ and non-disclosure of relevant data.⁴⁹ Re-analysis of the data of Dales et al.⁴³ has, in fact, identified a positive association for some children.”⁵⁰

A good example of poorly designed and analyzed MMR epidemiology is a recent study of Atlanta metropolitan area children.⁵¹ Here, the authors, from the CDC, chose to determine if there is an MMR-autism link by analyzing whether age of MMR vaccination impacted autism rates, even though MMR timing has never been hypothesized as a factor. Yet, the CDC authors chose *not* to analyze whether there was a higher rate of autism among those vaccinated versus those not vaccinated with MMR, even though there were enough in each group in the Atlanta cohort for statistical power to determine if a difference exists. In the meantime, the Atlanta database is off limits to other researchers who might want to examine this comparison. In the U.K., the data sets used to repudiate an MMR-autism connection have also been closed to outside epidemiologists.

The evidence against an association between thimerosal and autism has been almost exclusively epidemiological.⁵² The studies cited include one using the CDC’s Vaccine Safety DataLink (VSD),⁵³ one using a Danish registry of autistic children,⁵⁴ an unpublished study by health officials in the U.K.⁵⁵ and a study

using Swedish data by a CDC contractor.⁵⁶ The published VSD study reported no association between thimerosal and neurodevelopmental disorders, including autism. Yet earlier, unpublished versions of the data, obtained by advocates using the Freedom of Information Act, showed statistically significant associations and/or associations of sufficient strength to warrant further investigation. While public health officials point to this paper as ruling out a thimerosal-autism link, even the lead investigator, Thomas Verstraeten, who now works at vaccine maker GlaxoSmithKline, has said that the VSD analysis is insufficient to rule out an association.⁵⁷ The Danish study relied on incomplete registry data, so that new cases coming into the registry were not included in the analysis, thus skewing the results.⁵⁸ Several of the authors work for Staten Serum Institut, the Danish manufacturer of thimerosal vaccines and a major exporter of such vaccines into the U.S. The paper, using Swedish autism prevalence trends, relied solely on in-patient records, which constitute a small proportion of autism cases, rendering suspect any analysis of an autism-thimerosal association.⁵⁹ The British study has not been published and utilizes another closed database and thus cannot be evaluated or replicated.

The use of inadequate research programs to evaluate vaccine safety, illustrated in the case of MMR, thimerosal and autism, is indicative of a pattern. According to evidence-based medicine expert Dr. Thomas Jefferson, a strong vaccine supporter, “the design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate.”⁴⁵ Likewise, vaccine proponent Dr. Neal Halsey of the Vaccine Safety Institute explained to a trade publication that no one at the manufacturers or federal agencies had thought to calculate the amount of mercury being given to infants from vaccines, and added, “No one knows what dose of mercury, if any, from vaccines is safe. . . . We can say there is no evidence of harm, but the truth is no one has looked.”⁶⁰

Post-licensure safety assessment is handled primarily by the CDC and has relied almost exclusively on two data sets: the VSD and the Vaccine Adverse Event Reporting System (VAERS). VAERS is a passive reporting system and as such has been characterized as unre-

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liable and unscientific in identifying potential causal associations.⁶¹ The VSD is derived from automated HMO patient records and has been described by CDC staff as being able to generate at best weak associations which, if detected, would require further research.⁶² The VSD is a closed database, unavailable to independent researchers. Only CDC staff and their designated contractors are allowed to use this data set. The CDC has an inherent conflict of interest in assessing vaccine safety, since they are charged with approving the slate of recommended infant vaccines and increasing their uptake, as well as monitoring safety.⁶³ It would be difficult for CDC staff to admit to safety lapses if they were the ones who approved and promoted the vaccine in question. As Congressman Dave Weldon recently pointed out at a 2004 IOM vaccine safety review meeting, out of a billion-plus dollar budget to promote vaccine expansion, the CDC spends just 1-2% of their vaccine budget on safety. Thus, vaccine promotion receives far more weight at CDC than safety issues. Clearly, vaccine safety efforts need to be bolstered, and responsibility needs to be taken out of CDC and given to an independent agency with no inherent biases.

The autism increase is real and has reached epidemic proportions. We cannot afford, morally and financially, for so many of our citizens to be disabled. Parents are demanding credible research from unbiased sources. Parents are asking why biological studies show increasing evidence of an association between MMR and autism and thimerosal and autism, while the epidemiological assessments performed by government insiders and manufacturers appear to disprove a link.

It is not surprising that parents' trust in our immunization program is eroding. This development is alarming given the prominent role of vaccination in preventing infectious disease. But the solution is not to ignore compelling biological research and dishonestly disprove unpleasant theories through inadequate epidemiology. The solution is to conduct honest and rigorous investigations into vaccines' role in autism and related neurodevelopmental disorders, to open up taxpayer-supported databases to independent credentialed researchers, to develop better monitoring systems and to assign responsibility for vaccine safety to agencies without conflicts of interest. The solution also requires a new mindset for public health officials and vaccine manufacturers, away from one in which it is acceptable for a small number of

children to be harmed for the benefit of the greater good in the "war" against infectious disease, and toward one in which vaccine failures are seen as unacceptable, and precaution prevails. A first step in this direction would be the immediate removal of thimerosal from influenza vaccine now routinely recommended for our six- and seven-month-old babies. The 2004 flu season is just around the corner, and only 5 million of the 100 million doses of flu vaccine in production are being made without thimerosal, a situation blessed by our public officials at the CDC.

Sallie Bernard is executive director of the Coalition for Safe Minds, an autism advocacy group, and President, ARC Research. The parent of an autistic son, she is a board member of national Cure Autism Now Foundation, executive director of New Jersey Cure Autism Now and primary author of "Autism: A Unique Type of Mercury Poisoning." ■

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A Brief Reply from the Authors

First, Ms. Bernard states, "The MMR vaccine and the mercury-based vaccine preservative thimerosal [have been] both recently linked to autism..." However, little or no scientific support remains for what she presents as a given. We will let the readers decide for themselves between the conclusion by Ms. Bernard of an MMR and/or thimerosal etiology in autism and the opposing conclusion drawn by both the CDC and the IOM that the preponderance of evidence to date shows no connection between these two agents and autism.

Second, much of Ms. Bernard's case rests on conjuring up a shadowy conspiracy: e.g., "These studies, unfortunately, have mostly been conducted by CDC insiders or employees of vaccine manufacturers themselves and suffer from major methodological deficiencies. Moreover, the data sets relied on for a

number of these studies have been deliberately closed to other researchers, making replication of the findings impossible." Mixed in with salient criticism of the methodology of actual studies are implications of nefarious motives on the part of all the researchers who have reported against a vaccine link to autism.

Third, Ms. Bernard's claim that "In recognition of the weakness of research refuting an increase in incidence, the director of the CDC, Dr. Julie Gerberding, stated in a 2004 meeting with autism advocates that the weight of the evidence supports a true increase in the rate of autism" needs substantiation. It would have been helpful if Ms. Bernard had provided further details and a citation for this statement, apparently made behind closed doors, since it is used to buttress the very foundation of her thesis.

—Peter Thom and Shifra Krinshpun

In Search of Common Ground: A Survey of Publicly Sponsored Debate About Genetics and Reproduction

By Kathi E. Hanna

In the past 30 years, society has faced a steady progression of new advances in medically assisted reproduction and genetics that are considered everything from miraculous to immoral. In vitro fertilization (IVF) and other assisted reproductive technologies, prenatal diagnosis, pre-implantation genetic diagnosis, fetal tissue transplantation, prospects for germ-line gene transfer, human embryo research and now human cloning have increased the need for public discussions about difficult public policy choices. Many of these choices, although termed “bioethics,” are, in fact, social issues of considerable policy importance. They have substantial implications for decisions regarding research funding, legislative prohibitions, regulations, moratoria, healthcare financing and reimbursement.

Since 1974, numerous federal commissions, committees and panels have been created in the United States to deliberate a wide range of complex biomedical and ethical issues, of which reproductive technology and/or genetics have been consistent topics. Bioethics commissions offer an opportunity for mediating points of view among parties with differing levels and types of knowledge. The U.S. government’s forays into the realm of bioethics have had lasting impacts on the way society conducts biomedical research and delivers medical care. A brief history of each is presented below.

The National Commission

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission) was established in 1974. A series of research scandals, including the Tuskegee syphilis trials and testing of hormone analogues among welfare mothers and Mexican-American women, signaled to Congress that biomedical researchers were not adequately policing themselves and that some sort of oversight was necessary.

The National Commission was cre-

ated as part of the then Department of Health, Education, and Welfare (DHEW) and, fueled by the greater societal debate about elective abortion, research using the human fetus topped the agenda. Within four months of assuming office, the commissioners were mandated to report on the subject, with the proviso that the presentation of their report to the Secretary of DHEW would lift the moratorium that Congress had imposed on federal funding of research using live fetuses. In July 1975, the National Commission submitted its conclusions and recommendations in its report *Research on the Fetus*, which formed the basis for DHEW regulations on research involving fetuses, pregnant women and human IVF. Those regulations, 45 CFR 46, SubPart B, remain in place today.

When its charter expired, the Commission recommended that a successor body be created, with broader authority to address issues beyond protection of human participants in research. Issues regarding the safety of recombinant DNA were of concern, as was the termination of treatment (in the wake of the Karen Ann Quinlan case). Congress created a more general mandate for a national bioethics organization, the President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (the President’s Commission).

The President’s Commission

The President’s Commission was in operation from 1980 to 1983. It issued 11 reports, including one on genetic screening and counseling. A two-year debate about re-establishing the President’s Commission beyond its initial term began in November of 1982, when its report *Splicing Life* was released at a hearing before Albert Gore, Jr., then a member of the House of Representatives. The hearing focused on the implications of human genetics, particularly gene therapy. *Splicing Life* permitted policymakers and others to understand clearly that some cases of gene therapy would not be morally different from any other treatment, pointing to instances

where gene therapy might be technically preferable—and morally equivalent—to other treatments.

The President’s Commission recommended that the National Institutes of Health (NIH) review progress in gene therapy through its Recombinant DNA Advisory Committee (RAC), and that NIH consider the broad implications of commencing gene therapy. The RAC accepted this recommendation in April 1983 and “Points to Consider in the Design and Submission of Human Somatic Cell Gene Therapy Protocols” was adopted in 1986 as the keystone document in public oversight of the new technology.

Continuation of the President’s Commission was unacceptable to several conservative Senators, primarily because of their displeasure with the Commission’s recommendations about termination of treatment at the end of life. Senate conservatives wanted bioethics brought under direct Congressional scrutiny. The end result was the creation of an entirely new entity, the Biomedical Ethics Board, composed of members of Congress, and the Biomedical Ethics Advisory Committee, its operational arm.

The Biomedical Ethics Advisory Committee

The Biomedical Ethics Advisory Committee (BEAC) was a 14-member group whose multidisciplinary membership was appointed by the Biomedical Ethics Board (BEB), a process that consumed an inordinate amount of time. BEAC finally met in September 1988, less than a week before its authorization expired. Meanwhile, the BEB to which it was tethered sank deeper into the abortion debate. The first mandated report, on implications of human genetic engineering, stemmed from the original Gore bill proposing an extension of the President’s Commission. The deadline for the second report, on fetal research, expired before BEAC members were appointed. The fetal research mandate was reinstated in the Omnibus Health Extension Act of 1988 (P.L. 100-607) with the deadline delayed until November 1990. A

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third mandate focused on AIDS research and treatment.

The structure, never stable, began to disintegrate in March 1989, when the Senate Board members were unable to elect a chairman and found themselves in a partisan logjam along pro-choice/anti-abortion lines. BEAC died in the crossfire between the two factions and the office was closed at the end of September 1989, without ever having issued a report.

Deliberative Bodies Established at the Departmental Level

In 1975, the former DHEW announced it would fund no proposal for research on human embryos or on IVF, still an experimental technique, unless it was reviewed and approved by a federal ethics advisory board. Louise Brown, the first IVF baby, was born in Great Britain in 1978. The human subjects regulations that resulted from the National Commission's work required review of this type of research by an Ethics Advisory Board (EAB) to be appointed by the DHEW Secretary. In 1977, NIH received an application from an academic researcher for support of a study involving IVF. The NIH forwarded it to the EAB. At its May 1978 meeting, the EAB agreed to review the research proposal.

On May 4, 1979, in its report to the Secretary, the EAB concluded that federal support for IVF research was "acceptable from an ethical standpoint" provided that certain conditions were met, such as obtaining informed consent for the use of gametes and not maintaining an embryo "in vitro beyond the stage normally associated with the completion of implantation (14 days after fertilization)." No action was ever taken by the Secretary with respect to the board's report; for other reasons, the Department dissolved the EAB in 1980. Considerable opposition emanated from the Roman Catholic Church about the morality of IVF, which contributed to paralysis regarding reconstitution of the EAB.

Since it failed to appoint another EAB to consider additional research proposals, DHEW effectively forestalled any attempts to support IVF research, and no experimentation involving human embryos was ever federally funded pursuant to the conditions set forth in the May

1979 report or through any further EAB review.

The first Bush administration did not support re-establishing an EAB, thus extending a 12-year lapse in a federal mechanism for the review of controversial research protocols. This status continued until 1993, when the NIH Revitalization Act effectively ended the de facto moratorium on IVF and other types of research involving human embryos by nullifying the regulatory provision that mandated EAB review.

NIH's Human Embryo Research Panel

As the Revitalization Act of 1993 effectively ended the de facto moratorium on IVF and other types of research involving human embryos, the then NIH Director Harold Varmus convened a Human Embryo Research Panel (HERP) to develop standards for determining which projects could be funded ethically and which were "unacceptable for federal funding."

The panel of scientists, ethicists, legal scholars and lay representatives worked in an environment of heightened scrutiny by the anti-abortion lobby. The HERP submitted its report to the Advisory Committee to the NIH Director (ACD) in September 1994; included was a controversial recommendation that, under certain conditions, embryos could be created for research purposes.

Acting on this submission, the ACD formally approved the Panel's recommendations (including provision for the deliberate creation of research embryos). President Bill Clinton intervened to clarify his earlier endorsement of embryo research, stating that "I do not believe that federal funds should be used to support the *creation* of human embryos for research purposes, and I have directed that NIH not allocate any resources for such requests."

Director Varmus proceeded immediately to implement those HERP recommendations not proscribed by the President's clarification, concluding that NIH could begin to fund research activities involving "surplus" embryos. Before any funding decisions could be made, however, Congress took the opportunity afforded by the DHHS appropriations process to stipulate that any activity involving the creation, destruction or exposure to risk of injury or death to human embryos for research purposes may not be supported with federal funds

under any circumstances. Additional legislative riders have been inserted into subsequent annual DHHS appropriating statutes, enacting identically worded provisions into law. Thus, to date, no federal funds have been used for research that directly involves the deliberate creation or destruction of a human embryo. This issue would resurface in 1998 when the issue of human embryonic stem cells was addressed by NBAC (see page 13).

Human Fetal Tissue Transplantation Research Panel

During the 1980's, DHHS was grappling with another related and controversial issue. In 1988, Assistant Secretary Robert Windom requested that NIH convene a panel to advise him about the technical stakes and ethical implications of the use of fetal tissue in transplantation research funded by the federal government, specifically whether the moral issues surrounding the source of such tissue (elective abortions) could ethically be separated from the use to which such tissue is put (e.g., treatment of Parkinson's disease or diabetes). The majority of the appointed panel was in favor of permitting such research as long as three conditions were met in addition to IRB approval: (1) the decision to donate tissue was kept separate from and made only after the decision to abort; (2) the process for abortion was not altered in any way; and (3) the informed consent of both parents was obtained in cases when the fathers could be contacted. Panel members voted 19-2 to recommend continued funding for fetal tissue transplantation research under guidelines designed to ensure the ethical integrity of any experimental procedures. In November 1989, after the transition from the Reagan to the Bush administration, DHHS Secretary Louis Sullivan extended the moratorium indefinitely, based on the position taken by the minority-voting panel members that fetal tissue transplantation research would increase the incidence of elective abortion. Attempts by Congress to override the Secretary's decision were not enacted into law or were vetoed by President Bush.

In October 1992, a consortium of disease advocacy organizations filed suit against Secretary Sullivan, alleging that the Hyde Amendment (banning federal funding of abortion) did not apply to research or transplantation involving

In Search of Common Ground: A Survey of Publicly Sponsored Debate

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fetal tissue. The suit was preempted on January 22, 1993, when newly inaugurated President Bill Clinton shifted national biomedical policy and directed DHHS Secretary Donna Shalala to remove the ban on federal funding for human fetal tissue transplantation research. In March 1993, NIH published interim guidelines for research involving human fetal tissue transplantation. Provisions to legislate these safeguards were promptly proposed in Congress and included in the NIH Revitalization Act of 1993, which President Clinton signed into law on June 10, 1993.

The National Bioethics Advisory Commission

The National Bioethics Advisory Commission (NBAC) was established by President Clinton in 1995 to provide advice and make recommendations concerning bioethical issues arising in the context of government research programs. Four months into its existence and within days of the published report of Dolly, the cloned sheep, President Clinton instituted a ban on federal funding related to attempts to clone human beings. In addition, the President asked NBAC to address within 90 days the ethical and legal issues surrounding the subject of human cloning.

NBAC responded that, while the creation of embryos for research purposes alone always raises serious ethical questions, the use of somatic cell nuclear transfer to create embryos for research purposes raises no new issues. However, the unique and distinctive ethical issues raised by the use of somatic cell nuclear transfer to create children do raise new concerns, for example, serious safety issues, individuality, family integrity, and treating children as objects. The Commission concluded that the use of this technique to create a child would be a premature experiment that would expose the fetus and the developing child to unacceptable risks, which in itself might be sufficient to justify a prohibition on cloning human beings at this time, even if such efforts were to be characterized as the exercise of a fundamental right to attempt to procreate.

The Commission suggested that, in order to allow a further national discussion to take place, a period of time should be imposed during which no attempt is

made to create a child using somatic cell nuclear transfer. NBAC made an immediate request to all firms, clinicians, investigators and professional societies in the private and non-federally-funded sectors to comply voluntarily with the intent of the federal moratorium.

NBAC further recommended that federal legislation be enacted to prohibit anyone from attempting, whether in a research or clinical setting, to create a child through somatic cell nuclear transfer cloning and that any regulatory or legislative actions undertaken to effect the foregoing prohibition should be carefully written so as not to interfere with other important areas of scientific research. Despite several efforts in both chambers to legislate a ban on human cloning to produce a child, no laws have been passed, in part because of the inability of Congress to disentangle human cloning for reproductive purposes from cloning to derive embryonic stem (ES) cells for the purpose of research.

NBAC's Stem Cell Report

Scientific reports of the successful isolation and culture of ES cells and embryonic germ (EG) cells renewed the long-standing controversy about the ethics of research involving human embryos and cadaveric fetal material. Again, President Clinton turned to NBAC for guidance about the promise of these research developments as well as the ethical concerns. The Commission reiterated its previous position and re-emphasized that, at the current time, federal funds need not be used for such research. The President also asked NBAC to provide advice on the creation of human/non-human chimeras using somatic cell nuclear transfer, which would raise unique concerns.

NBAC stopped short of endorsing the use of somatic cell nuclear transfer to create an embryo for the purposes of deriving stem cells. Instead, it recommended that "at this time" federal funding for the use *and* derivation of ES and EG cells should be limited to two sources of such material: cadaveric fetal tissue and embryos remaining after infertility treatments. The Commission left open the possibility that these sources might prove insufficient and that the need for cloning to derive superior cell lines should be revisited after sufficient scientific work has been conducted to justify that further step.

In the background, a federal policy was already being crafted. When the question arose of whether to provide federal funding for human ES cell research using IVF embryos remaining from infertility treatments, the DHHS general counsel, Harriet Rabb, reported to the NIH director, Varmus, that the prohibition in the current appropriations rider did not prevent NIH from supporting research that uses ES cells derived from such a source because the cells themselves do not meet the statutory, medical or biological definition of a human embryo.

Having concluded that NIH may fund internal and external research that utilizes ES cells but does not create or actively destroy human embryos, NIH delayed actual funding until an Ad Hoc Working Group developed guidelines for the conduct of ethical research in this area. But time ran out. Before any grants could be funded, the infamous 2000 election results produced a new administration, and therefore new policies. In August 2001, President George W. Bush announced that NIH could fund research using ES cells, but only if the lines had been derived prior to that date; thus the federal government could not be considered complicit in the destruction of the embryos.

President's Council on Bioethics

At the end of the Clinton Administration, the charter for NBAC was allowed to expire in anticipation that the next President, whoever he might be, would want his own set of advisors and most likely a different charter. In November 2001, President George W. Bush named a new body, called the President's Council on Bioethics (PCB). The charter of the 18-member Council allows it to consider a range of bioethical matters connected with specific biomedical and technological activities, such as embryo and stem cell research, assisted reproduction, cloning, uses of knowledge and techniques derived from human genetics or the neurosciences, and end-of-life issues.

In its first report, *Human Cloning and Human Dignity: An Ethical Inquiry*, ten members of the PCB recommended a four-year moratorium on "cloning-for-biomedical-research." They also called for "a federal review of current and projected practices of human embryo research, pre-implantation genetic diagnosis, genetic modification of human em-

Barth Syndrome—Responding to a Genetic Disorder

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had been successful with the one living boy mentioned in the article who we could calculate would be older than our son. A kind response came back: "I agree that your patient may have the disease...." And then, "We regret that [the patient you asked about] died quite suddenly and unexpectedly while playing at home at the age of five." That one extended family had lost more than 20 sons, brothers, nephews and uncles over several generations to this disorder that was beginning to be called Barth syndrome. It was difficult to hear. For us, the good news was that Will's tentative diagnosis had been corroborated. The bad news was that our son might well be among the oldest living children with the condition, and the future did not seem at all bright. And that was all we knew.

With the caring treatment of his dedicated group of physicians, Will's condition improved and he came home. We began making regular follow-up trips to doctors' offices and endured several additional hospitalizations during the next few months. Because his disorder was so rare, no one was an expert. Will's care was centralized in one hospital, but we began to seek advice about the various aspects of Barth syndrome from specialists interested in complicated, unusual cases. These people were not located in any single facility or city. I counted recently that, during his lifetime, Will has seen physicians in 22 different medical specialties associated with 19 institutions.

It quickly became apparent that, beside Will, I was the only person who attended every appointment and was the lone keeper of his complete medical files. I became "command central" in many ways. There were times when I organized conference calls among his various doctors. I learned to request a copy of each test result and every office visit summary. I asked a lot of questions and bought a medical dictionary to help me understand what was said. Over time, my questions became more enlightened, and I became my son's primary advocate. My dedication, growing knowledge and easy access to all of his medical records gave me increasing credibility with his doctors. I learned the importance of mutual respect, and I gently but firmly established my own active role.

Will's disorder was rare—so rare that few physicians had ever heard of it be-

fore. Whenever he saw a new specialist, I took a copy of Dr. Barth's article to give to him/her. I usually knew more about the condition than the specialist did. Early on, Barth syndrome was not even listed in the National Organization for Rare Disorders (NORD) desk reference. And no one—not physicians, and certainly not our friends or family—knew of another patient with Barth syndrome. For 11 years, we became increasingly convinced that Will was the oldest living child with Barth syndrome. And Dr. Barth's experience with the family he knew in the Netherlands did not leave much room for optimism. Will continued to be monitored closely for his cardiomyopathy. He attended regular school and did many regular things, but his fluctuating immune system and his weak muscles made living a completely "normal" life difficult.

Advocacy: From Personal to Public

Over the years, we tried to find more information about Barth syndrome on the internet, but always with little success. Then, in November 1999, Will entered the words "Barth syndrome" into a search engine we had never used before, and the names and email addresses of three women appeared on the screen. Will was beside himself with excitement. My husband and I were elated, too, although we were leery of who these people might be. Were they researchers, salespeople, physicians, relatives of patients?

With our approval, Will contacted them. Within 24 hours, he received five emails—one from each of the women and two from their sons who had Barth syndrome. It was just before Thanksgiving; the internet had given us a gift for which we all will be eternally grateful. We later learned that these three mothers—Shelley, Sue and Anna—also had been searching the internet for someone else, anyone else, affected by Barth syndrome; they had found each other. With the help of Dr. Richard Kelley of Johns Hopkins and a very small budget donated by a loving grandmother, they were planning the first international meeting for Barth families and physicians to be held June 2000 in Baltimore, Maryland. It had long been a dream of Will's to meet another boy with Barth syndrome. We had to go.

Much could be written about that weekend. The desire to meet others struggling with the same problem

proved to be a very powerful incentive, and 28 families from four continents did whatever they had to do to be at that meeting—be it raising funds through car washes and local charities, driving 1200 miles or flying halfway around the world with a child whose health was precarious. There were endless discoveries made on every level. We all learned the power of sharing—not only tears and laughter, but also information. The boys were amazingly similar in numerous ways. The presence of so many grandparents with stories of boys lost in earlier generations made us all appreciate that our problems were not really new. We were beginning to understand the implications of a genetic disorder, to appreciate the strength that comes from community, to value the knowledge that each of us had to offer and to recognize the power of that knowledge when taken together. By the end of the weekend, we all knew that this had to be the beginning, not the end.

We needed an official organization. We would continue to rely on the internet to be the functional glue that would hold us together across thousands of miles, many time zones and numerous languages. After all, that was the *only* possible way we all could have first met. The internet had changed our lives, as it has so many others in similar situations. My husband and I volunteered to join the original three mothers to create a 501(c)(3) foundation to increase awareness among physicians, find and share information with more families and encourage research. We had no idea, really, what we were getting into, but we knew that we were dedicated to "saving lives through education, advances in treatment and pursuit of a cure"—and that is what counted.

My husband and I used our management training and sought the help of our friends and business colleagues to help figure out how to go about creating the nonprofit organization that we now call the Barth Syndrome Foundation, Inc. (BSF). We knew we could learn a great deal from other successful rare disorder foundations, and we received some guidance from the Genetic Alliance (www.geneticalliance.org) in identifying them. The five of us contacted every one of the foundations to find out what they had learned, what they had done right and what had not worked. One of our most important observations was that

Race and Genetics: Not a Matter of Black and White

By Peter Thom and
Sharmila Padukone

We need to adjust the number, to take things like diabetes, weight or race into account."

The genetic counselor explained the maternal serum screen to the patient and the student intern had to bite his tongue. "Race," as she was using the term, is, in our opinion, completely misleading, as is the term "black." In the American context, or to be more provincial yet, in the official U.S. context, "race" refers principally to European-Americans, African-Americans, Asian-Americans, Native Americans and Pacific Islanders. The term "black," on the other hand, because it is acceptable in a social context, has become synonymous with African-Americans and continues to be used, even among genetics professionals who should know better. In practice, this means that, in the American context, someone from the Solomon Islands or New Guinea would be lumped together with African-Americans as "black," solely on the basis of dark skin tone. However, in genetic terms, the assumption that dark-skinned people are similar, regardless of the geographical area of their family origin, is, at a minimum, imprecise.

Racial classifications have long been suspect, at least since Darwin's ideas began to take hold. Taxonomists have come up with various schemes defining anywhere from 3 to 60 distinct races. The depth of classification is completely arbitrary and, therefore, the predictive value of these taxonomies is mediocre at best.

For a long time, genetics professionals have accepted that genetic differences *within* any assigned group are larger than those *between* different groups. Further, as people all over the world become increasingly mobile, isolated populations are fast dying out. Mixing of gene pools is occurring at increasing rates, a factor that is having an impact on the value of even ethnicity as a predictor of genetic predisposition. The question then: can genetics professionals continue to use race as a basis for identifying genetic similarities or differences between populations?

Racial classification is by no means uniformly applied by medical and allied professionals. Splitting is limited to specific groups, while lumping is applied to others.

Consider the Europeans. When genetics professionals refer to European-Americans, the tendency is to split: i.e., to accept that there are known genetic differences between present-day Northern Europeans and Southern Europeans in terms of, among other things, susceptibility to various diseases. Italian-Americans and Greek-Americans, for example, are known to have greater susceptibility to thalassemias and have a different array of mutations for diseases common among Northern Europeans, such as cystic fibrosis. When counseling Americans with a European background, ethnicity is therefore always taken into account, and the concept of race is a secondary consideration, if at all.

Now consider what happens in the case of people of non-European origin. When the genetic makeup of African-Americans is discussed, all people (i.e., all people who are, for want of a more suitable word, "black") are lumped together. There are a number of very obvious problems with this sort of grouping: The vast territory of origin of African-Americans (Africa, far larger than the European landmass) is likely to have developed more, not less, genetic variation. Here, we must acknowledge that the great majority of African-Americans has lost the history of its ancestry, but that should in no way prevent genetics professionals from beginning to delineate present-day differences between people from various parts of Africa and applying that knowledge to African-Americans.

Asian-Americans face even more complex issues. Not only are Asian-Americans also lumped together regardless of whether they are of Chinese or Japanese or Nepali descent, but the people of South Asian descent are frequently ignored altogether! Thus, people of Indian, Pakistani or Sri Lankan descent are often not considered as a separate group at all, or are lumped together with the East Asians. Asia is the largest of the continents and contains more than

half the world's population. Need more be said with regard to the possibilities of genetic diversity?

When one remembers that there is a gradual but long overdue awareness of the increased dangers of elevated cholesterol and cardiac disease in the people of South Asian origin, the dangers of ignoring such ethnic diversity become glaringly apparent. How many more such conditions must be slipping through the cracks, and the unfortunate patients with them, even as you read this article?

There is a major problem, too, with accepting self-definitions of race. A self-professed African-American, for example, is statistically likely to be a product of an admixture of European and African genetic roots. The average African-American has a genetic contribution from Western Africa of 80%, but the range is anywhere from 20% to 100%. Nonetheless, due to the dominance of genes which express dark skin, that person will most often proclaim exclusive African ancestry. It is necessary, therefore, to probe beneath the surface of racial self-identification, beneath the skin, as it were. Perhaps the patient had a German grandmother who passed along a mutation for cystic fibrosis. Unless specifically teased out, this would remain hidden by the inaccurate self-identification. Many African-Americans, who could be carriers of diseases with a high frequency among their European ancestry, will be ill served unless the history of miscegenation is taken into account.

We would make a special plea to genetics professionals, indeed all medical professionals, to stop using the word "black" altogether. In fact, the disposal of the term "race" itself, along with all its connotations, is long overdue. Lumping people together by virtue of their skin color is not only misleading and disingenuous but also demeaning, especially coming from a group of professionals who should know better. How long will it be before these words are erased from our medical lexicon? A recent presentation downloaded from the National Society of Genetic Counselors referred to corrections in serum screening results that must be made for "blacks." We rest our case. ■

Barth Syndrome—Responding to a Genetic Disorder

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they were much more than just support groups. They had a positive vision of the future, and articulated goals and programs to address their problems. They were credible advocates for their causes. Our newly formed Board of Directors met in one member's kitchen to create our mission, vision and goals. We started by putting one foot in front of the next. We all agreed that, whatever we did, it would be with the highest level of professionalism possible. BSF was incorporated in the fall of 2000 and became an official non-profit organization in January 2001.

So far, we have been amazingly successful, and we are extremely grateful for our good fortune. We have published five significant, professional-looking newsletters with a distribution that now exceeds 3,000 contributors, patients, families, physicians and scientists. We have built an information-laden website (www.barthsyndrome.org) and manage several listserves, which are our daily lifelines. We have just hosted our third international Barth Scientific/Medical and Family Conference, which drew almost 250 family members, physicians and researchers and the largest group of affected individuals ever assembled. We have attracted a world-class Scientific and Medical Advisory Board and regularly attend scientific conferences, using our booth to distribute information to cardiologists, hematologists, neurologists, geneticists and pediatricians. And we recently have awarded our tenth research grant. This year, two international affiliates have been formed in Canada and the United Kingdom. These achievements have been possible through the \$1.3 million we have raised and a great deal of dedicated hard work on the part of volunteers. We have held fundraisers, written grants and found some generous sponsors. The positive momentum that can be created through the coming together of many different forces and resources is powerful. We try never to leave a stone unturned.

Although we have added Board members and gained helpers, we continue to be an all-volunteer organization, with the management still performed solely by Barth family members, at least to date. We are growing and evolving, but we feel that one of the limitations on what we can do is our ability to find enough volunteers to run all of the programs we would

like to create. Our Board will never stop working hard but is in constant danger of burning out; we know that this problem is typical. The wonderful thing is how broad our support is and how many volunteers we do have. And we marvel at how much help in various forms we receive from established institutions, including the National Institutes of Health (NIH), the American Heart Association, other disease groups and several large foundations. In every case, I believe it is because we continue to take seriously a few basic principles. We maintain high standards and do our homework in advance. We are a serious, professional organization run by people who do it as a labor of love. That is a powerful motivating force. BSF has become a credible advocate for our cause—just as we first learned to be for our own children.

Looking Ahead

Will is now 18 and a junior in high school. The nurses in the PICU know him by name because of his periodic admissions. In the past six months alone, he

has had an internal defibrillator implanted to guard against life-threatening arrhythmias, survived a blood clot in his heart and had a gastrostomy so that a feeding tube could be placed. Adolescence can be a very difficult period medically for boys with Barth syndrome... and so the fight goes on. But he continues to face his many adversities with courage, a positive attitude and even a sense of humor. He has become a remarkable young man. We now know that he is *not* the oldest living Barth patient, and we see scientific advancements (due in large part to BSF) being made that we expect will make a difference to his future. There are many more hurdles to overcome and dangers to conquer, but there are reasons to be cautiously hopeful, not just for him but for all Barth boys.

Kate McCurdy, a founding Board member of the BSF, serves as its Vice President of Science and Medicine. She has an MBA from Harvard and worked in the corporate world before her son was born. ■

WHAT IS BARTH SYNDROME?

Barth syndrome is a rare but serious, **x-linked genetic disorder** predominantly affecting males. It results from a mutation in the **G4.5 gene** (also called **TAZ1**) located at the distal end of Xq28. The cardinal clinical characteristics, which can appear in varying degrees, are:

- **Cardiomyopathy** (frequently dilated)
- **Neutropenia** (chronic, cyclic or intermittent)
- **Muscle hypoplasia and weakness**
- **Exercise intolerance**
- **Growth retardation** (can appear as Failure to Thrive)
- **3-Methyl-Gluconic Aciduria**

There is strong evidence that this disorder is not as rare as the initial statistics indicate. Many cases of this complex, multi-system disorder are mislabeled, with just a portion of the full syndrome being recognized.

But early full diagnosis is a key to survival. Preliminary data show that a boy whose diagnosis is missed has only a 30% chance of living to the age of four. With proper diagnosis at an early age, however, a child has an 85-90% chance of long-term survival.*

Several diagnostic laboratory tests are available. Further details regarding diagnosis criteria can be found at http://www.barthsyndrome.org/diagnose_barth_syndrome.html

*Source: The Barth Syndrome Foundation, Inc.

(Editors' note: X-linked diseases result from mutations on the X chromosome. A female inherits two X chromosomes, one from each parent, and can usually produce sufficient normal gene product, even with one mutated X chromosome, to be less affected or unaffected. A boy, however, inherits only one X chromosome, always from his mother, so, if his mother is a carrier, then he will be affected.)

Genetic Privacy: What's Happening at the Federal Level?

By Pat Banta

I have a conflict about describing the current federal rules and regulations related to genetic privacy. As an analyst in the executive branch of the federal government, do I tread lightly around a politically charged issue, or, as a health advocate, do I present a glimpse into the veiled world of regulatory doublespeak? Any reasonable civil servant working in governmental regulatory affairs comes to understand that the federal encyclopedia of law merely advises and rarely mandates. Federal entities are implicitly aware of their limited authority with respect to rule and regulation—the impunity of each state's sovereign right to rule its citizens. With that said...

A commentary found in an article about the Genetic Privacy Act offers a stunning metaphor on the need for genetic protection:

The highly personal nature of the information contained in DNA can be illustrated by thinking of DNA as containing an individual's "future diary." A diary is perhaps the most personal and private document a person can create. It contains a person's innermost thoughts and perceptions, and is usually hidden and locked to assure its secrecy. Diaries describe the past. The information in one's genetic code can be thought of as a coded probabilistic future diary because it describes an important part of a unique and personal future. (Annas & Elias, 1992).

Although genetics legislation has been in place in a few states since the 1970's, it was not until the 1990's, in an environment of increasing scholarly and media attention to genetic discrimination, that genetics statutes began to expand in scope and number. Initial genetics legislation was narrow, focusing primarily on genetic information associated with specific diseases. In the 1990's, states began to enact more sweeping laws. Responding to pressures from constituents and the scientific community, the federal government approached policy on an incremental level. In one sense, federal policy has begun to mimic the states' policy in that the protected genetic information is not disease specific but encompasses more general requirements. The next section describes

a federal effort toward genetic privacy in this arena of general requirements.

Federal Law Pertaining to Genetic Information Protection

The Health Insurance Portability and Accountability Act of 1996 (HIPAA), amends the Employee Retirement Income Security Act (ERISA), the Public Health Service Act (PHSA) and the Internal Revenue Code (IRC) to prohibit health discrimination on the basis of genetic information or services. Enforcement powers come through the Equal Employment Opportunity Commission (EEOC). HIPAA also requires the Secretary of the Department of Health and Human Services (DHHS) to develop policy recommendations and standards for protecting the privacy of individually identifiable health information from inappropriate use and disclosure. However, HIPAA does not specify what those standards should be or in what way they should address genetic information. The Secretary's resulting Privacy Rule, which came into effect on April 14, 2003, makes recommendations to treat genetic information as all other protected health information. The Privacy Rule does not preempt a state law if it is more stringent. There are many state laws that prevail over the Privacy Rule.

For health insurance in the group market, HIPAA does:

- Prohibit excluding an individual from group coverage because of past or present medical problems, including genetic information.
- Prohibit charging a higher premium to an individual as compared to others in the group.
- Limit exclusions from group health plans for pre-existing conditions to 12 months, and prohibit such exclusions if the individual has been previously covered for that condition for 12 months or more.
- State explicitly that genetic information in the absence of a current diagnosis of illness shall not be considered a preexisting condition.

HIPAA does not:

- Prohibit the use of genetic information as a basis for charging a group ad-

ditionally for health insurance.

- Limit the collection of genetic information by insurers or prohibit insurers from requiring an individual to take a genetic test.
- Limit the disclosure of genetic information by insurers.
- Apply to individual health insurers except if covered by the portability provision.

On October 14, 2003, the 108th Congress passed the Genetics Information Nondiscrimination Act (S.1053). This statute becomes effective in April 2005, 18 months after its enactment. As in HIPAA, this law will only address genetic discrimination as it relates to an individual's ability to obtain health insurance or employment. S.1053 is divided into two sections, one focusing on genetic discrimination in healthcare plans and coverage and the other focusing on the employment process. Both sections of the bill define genetic information as: (1) the genetic test of an individual; (2) the genetic tests of family members of the individual; (3) the occurrence of a disease or disorder in family members of the individual. The term "genetic information" does not include information on the gender or age of the individual. For human resources professionals in the higher education community, both the healthcare and employment sections of the bill will affect the administration of these areas.

Selected Legislation in the 108th Congress 1st and 2nd Session

The Patient Safety and Quality Improvement Act (H.R. 663, S. 720) amends the Public Health Service Act to make patient safety data privileged and confidential. The House version of the bill defines "patient safety work product" as a record concerning patient information either reported to a patient safety organization by a healthcare provider (doctor, hospital, etc.) or created by a patient safety organization. In addition, it defines a "patient safety organization" as an organization that collects such information with the goal of improving patient safety and the quality of healthcare delivery. The House adopted the act and ordered it reported to the Senate Com-

Eugenics, Reprogenetics and Newborn Screening: A Valuable Day of Discussion

By Erin M. Carter

Last February 19, Diane Paul, a recently retired professor of political science at the University of Massachusetts-Boston, visited Sarah Lawrence College. During a whirlwind day, she gave a presentation to the Science Seminar, "What is Wrong with Eugenics?"; conducted a HGP ethics seminar on newborn screening for phenylketonuria (PKU); and participated in a HAP class. Paul's work combines public policy with the sociology of science and moral philosophy. As she became interested in genetics, she returned to school herself to become better educated in the biological sciences and genomics. She has written two books, *Controlling Human Heredity: 1865 to the Present* and *The Politics of Heredity: Essays on Eugenics, Biomedicine, and the Nature-Nurture Debate*; has edited one book, *Thinking about Evolution: Historical, Philosophical, and Political Perspectives*; and has authored more than 100 other publications.

Eugenics itself is a term with a heavily contested definition, one that has taken on different meanings in different eras. Today, the word can evoke stories of Nazi Germany, Aldous Huxley's *Brave New World*, racial and/or class prejudice, negative attitudes toward people with disabilities and violation of the principle of respect for autonomy. Paul's work on the history of eugenics policy reminds us that well-known and very highly regarded scientists, including Linus Pauling, supported eugenics policies that would "improve" the human race. It is important to recognize that questions raised by the eugenics movements in the past remain significant in today's debate about the choices available in reproductive genetics. Paul notes that, although the word "eugenics" is generally shunned in contemporary society, "...many practices that would presumptively constitute eugenics, such as laws barring marriages between first cousins, are applauded. So I think we tend to apply the label to policies/practices/ideas we detest, and withhold it from those we approve."

Paul's recent research includes an exploration of the ways in which the history of eugenics figures in current de-

bates over reproductive genetics. In the mid 1990's, the term "reprogenetics" was coined to classify the variety of genetic techniques used to alter or control the reproductive process (Silver, 1997). Reprogenetic technologies allow us to treat infertility and strive toward the elimination of preventable genetic diseases, such as cystic fibrosis, sickle cell anemia, and PKU. However, reprogenetics is also the science behind so-called "designer babies."

Findings of genetic research appear in the news on a daily basis. Often, research breakthroughs have immediate ethical ramifications, and the public is unprepared for the outcomes. It is true that remarkable advances in science and technology are leading to a reconsideration of long-held ideas regarding parenthood, childhood and the meaning of life. Paul does not think it is possible to talk of a "public" attitude toward reprogenetics: "Even if we substituted a term like 'reproductive genetic technology' or 'genetic technology'...I think there are many different publics, with very different orientations."

Paul is currently writing a policy-oriented history of newborn screening for metabolic disorders, such as PKU. She spent the afternoon of her visit speaking with Human Genetics students regarding some of the complexities of PKU

screening. "[Newborn screening] is a springboard to discuss an array of bio-ethical and policy issues in genetic testing," she says, "including debates over the value of informed consent and the intersecting roles played by a 'technological imperative,' commercial interests and parent and patient advocacy groups in driving the expansion of screening."

Newborn screening began in Buffalo, New York, in 1960, with the invention of a cheap and simple blood test for PKU, a rare genetic condition that negatively affects the body's ability to break down phenylalanine, an essential amino acid found in nearly all foods. Without therapy, a person with PKU accumulates high levels of phenylalanine in the body, resulting in severe mental retardation and behavior problems. If detected early, symptoms of PKU can be prevented by lifelong adherence to a diet restricted to phenylalanine-free food.

PKU screening is now identified as the prototype of a successful screening program, but Paul's analysis finds even PKU screening to have a more complicated outcome. Pregnant women with PKU may have impaired intellectual capabilities as a result of not following the restrictive diet, thereby also impairing their ability to give informed consent

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The Program in Narrative Medicine at Columbia College of Physicians and Surgeons
Presents

"Suffering, Storytelling, and Community"

Thursday, October 7

Columbia University Medical Center

Plenary Lecture, John Stone, 1:00 – 2:00 p.m.

John Stone, MD, is Professor of Medicine Emeritus at Emory University School of Medicine, where he was also Director of Admissions and Associate Dean for 19 years. The author of four poetry volumes and an essay collection, *In the Country of Hearts: Journeys in the Art of Medicine*, he is also co-editor of *On Doctoring*. His most recent book is *Music from Apartment 8: New and Selected Poems*.

Workshops (leaders to be announced), 2:30 – 4:30 p.m.

Narrative Medicine Rounds and Reception, Arthur Frank, 5:00 – 6:30 p.m.

Arthur Frank, PhD., Professor of Sociology, University of Calgary, is the author of *The Wounded Storyteller, At the Will of the Body: Reflections on Illness* and of the recently published *The Renewal Of Generosity: Illness, Medicine, and How to Live*.

Free and open to the public. Same-day conference and workshop registration. For more information, call (212) 305-4975. For directions, please visit <http://cumc.columbia.edu/hs/map.html>. This event is made possible by the generous support of the New York Council for the Humanities, a state affiliate of the National Endowment for the Humanities.

Co-sponsored by the Health Advocacy Program at Sarah Lawrence College.

Genetics and Health Advocacy: A Dual Degree for 21st Century Healthcare

By Rachel Grob

Medicine is focusing increasingly on the genetic components of disease and of personal risk for complex disorders. Across the multiple sectors of our healthcare system, more and more resources are devoted to genetic issues, from mass screening for genetic disease to extensive research on the human genome to ever-more-elaborate forms of prenatal intervention. Media attention on issues ranging from how to protect the privacy of genetic information to whether it is appropriate to use technology to create "designer babies" has brought complex policy issues into the public arena. In short, the future of health care is intimately connected to genomic medicine, and the future of genetics is inextricably linked to a series of complex ethical, social and legal issues calling out for professional advocacy. The time for "Genetic Health Advocates" has never been riper.

Sarah Lawrence is proud to respond to the social need for professionals educated broadly across the fields of human genetics and health advocacy by offering a dual degree. This three-year program leads to a double master's, MA (from the Health Advocacy Program, HAP) and MS (from the Human Genetics Program, HGP). By blending curricula from the two programs, the dual degree offers students the opportunity to build a unique complement of knowledge, skills and competencies. The HGP's scientific rigor, extensive focus on interpersonal communication and sensitivity to psychosocial issues is well complemented by the HAP's attention to social, political and historical context, individual and collective rights, construction of knowledge, and the range of advocacy models and roles. Since faculty teaching in the areas of illness narratives, ethics and evaluation/assessment already bridges the two programs, these areas of overlap are easily navigated. Lectures, visiting scholars, films and other co-curricular offerings are also jointly coordinated, benefiting all students in each program as well as dual-degree enrollees. In typical Sarah Lawrence style, the three-year program is custom designed—in terms of schedules, internships/placements and sequence of courses—to accommodate the

needs of each dual-degree student.

What are dual-degree graduates equipped to do? We believe they have the best available preparation to work in public sector departments, healthcare settings, research institutions, not-for-profit organizations and industry, addressing a wide range of social and ethical issues such as:

- How can research agendas be shaped to expand knowledge while, at the same time, protecting human subjects and providing adequate support for study participants?
- How can individual and collective patient's rights best be protected—both in the United States and internationally—in an era of expanded genetic screening and testing? How can freedom of choice and access to information and counseling be preserved in the face of broad-based screening programs?
- How can an understanding of environmental and social factors in disease causation be balanced with an increasingly powerful analysis of genetic causation?
- How can debate about the uses of genetic science and information be fostered across broad segments of the population, and how can decision-making about the use of genetics in society be democratized?
- How can the gaps between expert and lay knowledge of genetics be bridged, and how can issues of race, ethnicity and culture be adequately addressed within the field of genetic counseling and beyond?

To Meg Howard's rallying cry "Ad-

HAP To Launch Conference Series

Through a series of annual conferences, the Health Advocacy Program will bring together advocacy groups from across the spectrum of disease-specific and issue-focused organizations to address critical issues of concern to all health advocates, analyze successful models of advocacy and forge alliances to work together to promote common goals. The inaugural conference, scheduled for January 14, 2005 at Sarah Lawrence, will be devoted to the issue of Advocates in Research. This full-day conference will include plenaries and breakout workshop sessions. Participants will be invited from a broad range of advocacy groups. The conference will provide an extraordinary opportunity to initiate dialogue among advocates so that we may learn from each other and work together to achieve common goals.

vocates and Genetic Counselors, Unite!" we might add the exclamation "Genetic Health Advocates, Your Time is Here!" We look forward to following the careers of the first dual-degree pioneers, and to attracting additional enrollees interested in the opportunities and challenges of Genetic Health Advocacy.

Rachel Grob, HA '92, is SLC Associate Dean of Graduate Studies and co-teacher of the HAP course *Models of Advocacy: Theory and Practice*. ■

Autism: Piecing the Puzzle—Together

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Advocates and Genetic Counselors, Unite!

An Internship at The March of Dimes Pregnancy and Newborn Health Resource Center Lays the Foundation for Future Genetics Advocacy Initiatives

By Meghan Howard

My recent internship at the March of Dimes Pregnancy and Newborn Health Education Resource Center gave me an opportunity to act as a link between the medical community and the general public. As an assistant information specialist, I researched and responded to emails received by the Resource Center. Inquiries covered a wide array of topics, from fears about worrisome pregnancy symptoms to descriptions of very specific genetic mutations and questions about their potential phenotypic implications.

Many of these emails exposed major weaknesses in our healthcare system. First, they drove home the fact that far too many people do not have access to healthcare because they cannot afford insurance and are ineligible for government programs such as Medicaid and Medicare. Second, they revealed that patients lack relationships with their healthcare providers that would allow them to express their personal concerns or to become appropriately educated about their health. Third, recurrent inquiries about genetics information indicated that, despite recent and continuing advances in genetic and reproductive science, the average individual remains grossly unaware of this technology and, in many cases, ignorant of even basic genetic and reproductive concepts.

Although I had realized previously that such problems existed, my internship at the March of Dimes provided a direct connection with individuals whose lives have been negatively impacted by them. This experience strengthened my conviction that professionals trained in both genetics and advocacy are desperately needed to bridge the perilously wide gaps that currently lie between the medical community, legislators and the public.

In this article, I will describe three types of very poignant emails to which I repeatedly responded during my time at the March of Dimes. By identifying the unmet needs of the emailers and then describing the ways in which the staff at the Resource Center provides services to those individuals, I hope to develop a general framework from which future

genetic advocacy initiatives may take shape. Finally, I will comment on my learning experience at the March of Dimes from the perspective of understanding some of the more controversial questions about the place of values and ethical perspectives in the work of the advocate and the counselor.

Helping the Uninsured

One of the most disturbing aspects about the inadequacies of health insurance coverage in the United States is that many of the uncovered are pregnant women. Despite many states' efforts to expand Medicaid eligibility to include larger numbers of pregnant women or to develop aid programs that specifically target this vulnerable and medically needy group, a frightening number continue to fall through the cracks.

During my time at the Pregnancy and Newborn Resource Center, I learned that these unfortunate women come from all walks of life. Illegal immigrants, the unemployed, working mothers unable to afford adequate insurance, and newly employed women whose insurance companies cited their pregnancies as pre-existing conditions—all contact the March of Dimes requesting assistance to cover the cost of childbearing.

After receiving this type of email, we usually did some research to investigate Medicaid requirements for the state in question and identify other types of resources (government or privately funded) available to assist pregnant women in that state. In situations where government assistance simply is not available to an uninsured pregnant woman, it is important to find other ways to provide access to prenatal care. Therefore, we always supplied such women with a list of free or low-cost healthcare clinics in their area.

The importance of prenatal care is well known to those in the field of genetics. Women who see a healthcare provider regularly during pregnancy have healthier babies and are less likely to deliver prematurely and/or have other serious problems, including infants with birth defects. Therefore, genetic advocates appear to be the perfect professionals to encourage prenatal care and to fight for all women to have access to it.

Filling Gaps in the Patient-Provider Relationship

Many of the emails received by the Resource Center disclose people's deepest fears, concerns and feelings of guilt. Teenagers admit to having had sexual intercourse for the first time, pregnant women express guilt over having indulged in alcohol or drugs during their pregnancies and family members describe symptoms that they fear may indicate genetic disease.

These are subjects that many individuals are uncomfortable discussing with anyone. It is not surprising, therefore, that they often choose to disclose such personal information via email rather than in face-to-face interactions, or even over the phone. However, the inconsistency that most consumers experience with regard to their healthcare providers can only reduce the likelihood that those needing services related to potentially embarrassing subjects will seek treatment or consultation. Worse, they do not often receive any education on such topics, leading to confusion and fear when personal problems arise.

Unfortunately, many of these emails involve problems that require immediate attention. Although the March of Dimes does not recommend or endorse any specific healthcare providers, we usually replied with a list of nearby hospitals or specialists and the suggestion that the emailer seek medical attention as soon as possible.

If "genetic advocates" had been available to provide educational services specific to reproductive health and pregnancy, many of these desperate patients would have known to seek the medical attention that they needed much sooner.

Providing Genetic Education

Some of the most common emails received at the Resource Center are those asking for information on a specific birth defect or inquiring about other genetic issues. Many of these come from parents of new babies with recently diagnosed genetic conditions, others from couples considering pregnancy but concerned about either inherited familial traits or risk factors such as maternal age. We usually responded to these inquiries by providing basic information about top-

Advocates and Genetic Counselors, Unite!

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ics such as chromosomes and inheritance patterns, along with a description of genetic counseling services and how they can be obtained. We often included a list of genetic support groups and resources.

For those whose lives have been touched by genetic disease, such genetic services are very important. However, although they are gradually expanding in number, these resources remain largely unknown to many healthcare providers, including physicians, social workers and even geneticists. This situation provides a perfect instance in which the genetic advocate could improve the healthcare experience of many by educating healthcare professionals about the importance of genetic support groups and resources.

A Framework for Action

In some ways, the March of Dimes is already filling the role of the genetic advocate. By providing patient education on topics related to reproductive health and genetics, and by disseminating information about financial and social support services, it certainly is addressing some of the critical problems that our current healthcare system so often neglects.

Representatives from the March of Dimes regularly give testimony at national hearings on topics related to pregnancy, health policy and genetics. The March of Dimes also funds research on various subjects pertinent to genetic and reproductive health. Its work has laid the foundation upon which further advocacy projects can be built.

The role of the genetic counselor is

expanding rapidly. Simultaneously, the field of advocacy is growing in breadth and impact. Without question, there is an overlap between these two professions. It seems likely that, as technology progresses and genetic services become more accessible, the need for a new specialist position combining the strengths of both advocacy and genetic counseling will emerge as a sort of "genetic advocate." By helping families to make informed reproductive choices, advocating for those affected with genetic conditions, and educating our political leaders, legislators and the general public, genetic advocates may be able to improve significantly the responsiveness and effectiveness of our healthcare system.

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Genetic Privacy: What's Happening at the Federal Level

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mittee on Health, Education, Labor and Pensions on July 23, 2003. On November 17, 2003 it was placed on the Senate legislative calendar.

This act, should it become law, includes provisions in both the House and Senate versions that have an impact on genetic privacy. These provisions:

- Require the DHHS to develop or adopt voluntary national standards for promoting the integration of healthcare information technology systems.

- Permit disclosures necessary for the proper management and administration of the patient safety organization, including maintenance of a patient's medical record, in a disciplinary proceeding relating to a provider, or as needed by the Food and Drug Administration (FDA) for regulatory purposes.

- Require the HHS Secretary to develop or adopt voluntary national standards promoting the integration of healthcare information technology systems.

- Require the HHS Secretary to contract for and report to Congress on a study assessing the impact of medical technologies and therapies on patient safety and benefit, healthcare quality and costs, as well as productivity growth.

- Amend the Social Security Act to direct the Secretary to appoint a Medical Information Technology Advisory

Board (MITAB) and direct the MITAB to make recommendations to the Secretary regarding medical information technology, including: (1) the best current practices in medical information technology and (2) methods of implementing records security.

The Human Cloning Prohibition Act of 2003 (H.R. 534; S. 245) was adopted by the House in March 2003 and referred to the Senate Committee on Health, Education, Labor and Pensions on January 29, 2003. If signed into law, it would make cloning a human embryo illegal, ban the importation of a cloned embryo or any product derived from one and impose fines and imprisonment for violators.

Genetics-Specific Legislation— A Personal View

In the rush to identify and focus on the social implications of genetic privacy legislation, I believe policymakers skip over obvious questions. Because of this, it is important for advocates and genetic counselors to ask the following questions. Is there anything new here? Does this present a different genre of social and ethical issues? Alternatively, does recently developed technology ask us to re-examine long-standing confidentiality issues that have never been truly resolved?

Specifically, legislators should be attentive to the serious inequities of genet-

ics-specific legislation and, in the spirit of the moral and policy values surrounding the Equal Protection clause, should broaden the nondiscrimination and privacy protections to include all medical information (Suter, 2001). Perhaps a legislative strategy that re-conceptualizes the problems and shifts the focus on genetics to those features of medical information that render it susceptible to discrimination and invasion of privacy would be more equitable, coherent and just. Health advocates, genetic counselors and other healthcare professionals should become active voices in this debate and work to inform legislators of the need for a comprehensive rather than an incremental approach to policy related to confidentiality issues.

Pat Banta, HA'00, assumed a new position in August as manager of government grants at the Visiting Nurse Service of New York. Prior to that, she was a senior program analyst at the Office of Inspector General, Office of Evaluation and Inspections, during which time she wrote this article. ■

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Clinical Research and Tissue Banking: An Ethics Perspective

By Alice Herb

My occasional articles for the *Bulletin* are meant to review bioethical issues occurring in the clinical setting. Sharing a case history with its dilemmas, its ethical issues and its outcome is a graphic way of emphasizing the importance of bioethical principles and the need for advocacy in medicine. This time there is no case, but I hope an equally engaging topic: the dilemmas surrounding the retention and storage of blood samples or other tissue specimen collected in a clinical trial.

Tissue banking is a hot-button topic for me as an IRB (Institutional Review Board) member. Before telling you why this issue has become so important, however, let me digress to explain what an IRB does. An IRB is an independent or free-standing committee that reviews research protocols at medical or other facilities; its main mission is the protection of human subjects. In submitting applications for IRB approval, researchers, or Principal Investigators (PIs), must reveal what they propose to do—including what precisely will be done to, for or with the *human subject*. I have italicized *human subject* so that we always bear in mind that prevention of harm is critical.

Among the many items to be filled out in the application for IRB approval is one that states whether or not blood or other tissue specimen are to be collected and how these specimen are to be used. Most often, blood drawing or biopsies are done for diagnostic purposes, but, when the person is also a research subject, the leftover samples become important research material. These samples belong to the donor, however, and what is to be done with them should be determined by the person giving them. It is essential, therefore, that the potential participant be informed of her rights and the implications of using specimen for research. The word “informed” is operative because the purpose and use of these specimen should be clearly stated in the *Informed Consent* draft that is included in the application packet and should as well be explicitly explained by the PI to the recruit.

But why do we care? The blood has been drawn; the biopsies done. Who cares? We do need to care because this is

no longer simply a donation of what would otherwise be discarded. Technology now enables us to identify a person by her unique DNA. Each sample collected bears the unmistakable mark of that donor. Thus, protection of the donor’s confidentiality becomes a major concern.

Confidentiality is a very fragile concept in this electronic age, even with HIPAA (Health Insurance Portability and Accountability Act) legislation that attempts to protect a patient’s health information from unauthorized electronic transmission. Too many people can access information that could be damaging in terms of insurance, employment and even criminal investigations. Information on genetic markers, genetic predispositions or genetic patterns can now easily be extracted from the samples and perhaps bring untoward difficulties or embarrassment for the research subject, and possibly even her family. For these reasons, each person faced with donating samples should be fully aware of the risks involved. So back to the necessity for informed consent.

Since informed consent is an integral element in the IRB approval process, it is at this pre-approval stage that the options for consent to the various uses for the specimen need to be spelled out. Let us suppose that the potential recruit decides that the quest for scientific knowledge is worth the risk of an unwarranted violation of confidentiality. She is altruistic or wants to know more about her disease and is willing to allow scientists/physicians to use her specimen for exploration into that disease. She might even be willing to agree to research into all cancers or into any disease. But would she be willing to have her specimen made into a cell line that might be patented and ultimately used for commercial purposes with the clear understanding that she will not share in the profits? She might. You might. But I may not. These specific choices should be individually and clearly stated and explained in the consent process giving the potential subject the option of consent or refusal for each option.

One other element that may influence a consent or refusal is whether the sample can be stripped of its identification. If

new findings are not going to be communicated to the donor, one would question why any linkage needs to be maintained. In order to provide confidentiality, PIs routinely assign a number or other symbol to the specimen and the PI commits to keeping the identification under lock and key. But even this linkage can be risky for the donor since research sponsors, federal, state and local officials and others may under certain circumstances have access to the genetic information. Even double coding, giving one more layer of protection, does not guarantee confidentiality. Destroying identifiers, however, can offer the desired anonymity. PIs may insist that for certain research linkage is essential. Under these circumstances, it behooves PIs to explain why.

We must, therefore, be reminded that even one drop of blood cannot be retained without permission and that confidentiality and privacy remain vital concepts in protecting us from unwarranted intrusions. Potential research participants may indeed opt to overlook confidentiality risks. That is their right. The motivation to contribute to science by agreeing to the banking of tissue/blood for future research may in fact prevail. But informed decisions cannot be made unless all of the salient information—including the individual’s rights to the disposition of blood and tissue samples and the risks to confidentiality and privacy—is provided. The participant’s free and voluntary choice to agree to tissue storage should be based on her understanding of what she is doing, i.e., with full notice and disclosure.

For more specific information, see the National Institutes of Health (NIH) training website Office of Human Subject Research (OHSR) fact sheets: <http://www.nihtraining.com/ohsr/info/sheet14.html>, <http://www.nihtraining.com/ohsr/info/sheet15.html>

Alice Herb, JD, LL.M., is a member of the HAP and HGP faculties at Sarah Lawrence. An attorney and bioethicist, she teaches bioethics to graduate students at SLC and to medical students at Downstate Medical School (SUNY). Her interests include human subject protection and end-of-life decisions. ■

Vaccine Safety and Autism: The System is "Broke," Let's Fix it

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In Search of Common Ground: A Survey of Publicly Sponsored Debate

Continued from page 13

bryos and gametes and related matters, with a view to recommending and shaping ethically sound policies for the entire field." Its advocates argued that a moratorium "would provide the time and incentive required to develop a system of national regulation that might come into use if, at the end of the four-year period, the moratorium were not reinstated or made permanent." They contended further that, "In the absence of a moratorium, few proponents of the research would have much incentive to institute an effective regulatory system."

Seven members of the 18-member council (one abstained) voted for "permitting cloning-for-biomedical-research now, while governing it through a prudent and sensible regulatory regime." They advocated that allowing research to

go forward could only occur when the necessary regulatory protections to avoid abuses and misuses of cloned embryos are in place. "These regulations might touch on the secure handling of embryos, licensing and prior review of research projects, the protection of egg donors, and the provision of equal access to benefits."

The Council has added sex selection, genetic enhancement and patenting human life to its future topics.

Lessons Learned

The National Commission, the President's Commission, the EAB, BEAC, NBAC and the PCB were all national responses to the need for a mechanism to address contentious issues in the practice of medicine and the conduct of biomedical research. This would suggest that policymakers recognize the need for a federal effort comprising diversely

trained individuals to monitor the interface between ethics and medicine. In theory, such bodies are charged with the responsibility of informing legislators, regulators, adjudicators, healthcare providers, scientists and the lay public about principles to be considered when making difficult decisions in medicine and biomedical research. National commissions allow debates about controversial topics to go forward in a somewhat less politicized way than is possible on the floors of Congress or on the center stage of the White House.

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Advocates and Genetic Counselors, Unite!

Continued from page 21

Reflection on the Internship Experience

Working as an intern at the March of Dimes reinforced my belief that genetics and advocacy are interrelated in ways important both to individuals and to policy. But it also immersed me in the world of contradictions and compromises that can accompany advocacy work. In our models class last semester, we kept coming back to the question of idealism vs. realism and how to balance these when striving to reach advocacy objectives. For example, we had some speakers who explained that, in order to be effective in their advocacy efforts, they had to limit their focus to just one specific issue or make other compromises along the way.

During my tenure at the March of Dimes, I had a good opportunity to confront precisely this tension as I sometimes became extremely frustrated by the organization's position of "neutrality" on controversial topics—topics about which I am most passionate: reproductive rights, stem cell research, fetal tissue research, sex selection and abortion. In the Resource Center, when I was asked questions concerning these or any other potentially sensitive issues, I could merely respond with the simple statement "The March of Dimes does not

provide information on this issue."

My reaction to working within this information restriction seesawed. At first, I was interested to learn about the workings of such a successful institution, and happy to be able to answer the questions that I could. As time progressed, however, it became increasingly difficult for me to ignore the pleas of young girls seeking pregnancy termination information, parents inquiring about stem cell treatment options and countless other desperate emails, letters, and phone calls from people seeking information that I was not allowed to provide. Eventually, I came to realize that the research, public health advocacy, and pregnancy education that the March of Dimes provides might not be possible without this compromise. Their funding, for example, comes from many religious and cultural groups that might take those dollars away if the March of Dimes moved even a fraction of an inch in either direction of its currently neutral positions. Effectiveness in a narrow area, I reasoned, might be an equally ethical choice. But this argument only works if there really is such a choice as "neutrality."

When it came time for me to complete my final project, a presentation entitled "Pregnancy Over 40 and Beyond: Guidance and Information for Mature Mothers and Mothers-To-Be," I learned that I could not be "neutral" in my work, nor,

I felt, could an organization, including the March of Dimes. My presentation included information about the biological and genetic risks associated with pregnancy later in life, as well as the social and psychological implications of being an older parent. Rather than taking a stance of neutrality, I asserted that there simply is not enough balanced and accurate information available to women who decide to have children later in life. I also proposed that the information that is available to this group often implies that women have a responsibility to have babies earlier in life, when they are in their "prime," despite the fact that the second decade of life is simply not the ideal child-bearing decade—socially, financially or psychologically—for increasing numbers of modern women in this country and many others.

Numerous March of Dimes staff members who attended my lecture challenged the notion that it should be a woman's choice to determine when she has a baby. One woman (a physician) even expressed her opinion that the March of Dimes should actually put out a publication *discouraging* women from giving birth over the age of 35 because the slightly increased risk of birth defects is in direct conflict with the March of Dimes' mission to "save... and improve the lives of babies."

Researching Genetic Conditions on the Internet

By Paige Hankins

A huge amount of genetic information is available on the web. Before diving in, however, it is important to define one's motives for research. Most often, people are interested in general education (e.g., academic requirement or curiosity), obtaining information about a genetic condition affecting self or family, or obtaining such information when self or family is at risk.

Identifying the reason for one's interest in genetics provides focus and direction to the search. In general, there are three principal types of information:

- Research concerning physical features and symptoms is helpful in looking for and recognizing manifestations of a disorder.
- Knowledge about the physiology of a genetic disorder aids in understanding how it can occur. Often people are unaware of, or misinformed about, the causes of a genetic condition.
- Support group websites for specific genetic disorders can be beneficial not only for the patient, but for friends and family as well. While they do not necessarily offer accurate and reliable facts, they do help individuals not to feel so alone during a difficult time.

Where to Obtain Information

The vast amount of information on the web can be overwhelming—even to professionals. It is important to be able to sift effectively through this mass of data to obtain accurate information relevant to one's needs. Search engines are an acceptable starting point; however, it is useful to limit a search to obtain relevant and accurate websites. Use an engine that allows for Boolean operators, simple words such as "and," "or" and "not" that define the relationships between keywords. Other features such as specific field searches, adjacency, proximity, truncation and plain English can also be helpful in narrowing the search results.

The table below lists genetic websites

http://www.ncbi.nlm.nih.gov	OMIM, PubMed (Medline)
http://www.geneticalliance.org	Genetic Alliance: Diseases resource, contact information on over 300 support groups
http://jama.ama-assn.org	Journal of the American Medical Association: Research articles
http://www.modimes.org/	March of Dimes: Birth defects, pregnancy, newborn care, support groups
http://www.pdrhealth.com	Physician's Desk Reference: Drug information, disease overviews
http://www.rarediseases.org	National Organization of Rare Disorders (NORD): Large disease database

considered reliable for research purposes. The first entry, the NCBI website, is a widely used and reliable resource. It includes information from PubMed, biomedical literature via the National Library of Medicine, and OMIM, the Online Mendelian Inheritance of Man that catalogs human disorders and genes. Many other research-based websites actually use the NCBI resource for their articles. In Medline, there are a variety of options available to help focus a search—a specific paper, an answer to a genetic question or general information about a topic. It also has an option to help those who are unsure about where to begin searching, or even to broaden a search to other databases.

How to Spot Nonsense

As the internet is open to the general public and is not screened or filtered through publishers, almost anything can be posted on the web. The benefit of this free flow of information is that the public has immediate access to information; the downside is that the accuracy of the material is often questionable. It is important to be able to distinguish good, accurate information from that which is faulty or misleading. In any article, cited references are a must. This is simply confirmation that other studies or articles have used similar data and/or come to similar conclusions. When researching, it is best to stay with well-known organizations and websites. Typically, their data is more widely referred to and critiqued. Editorial articles and chat rooms can be interesting and enlightening, but should not be deemed accurate information. Any information obtained on one of these sites should be confirmed using research data from a more solid source.

Even when reading an article from a scientific journal or study, there are several questions that should help determine if the test method was valid. Take note of the "methods" section of the article. Its design is most important in determining whether the article is sound

and significant. The following questions will help in that process.

- Was the study original? It can be similar to others, but, if so, does the new research add to the literature in any way?
- Who is the study about? How were subjects chosen? Who was excluded/included? What was the environment in which the subjects were tested?
- Was the study design sensible? If testing drug treatment and/or medical intervention, was it a double-blind, randomized, controlled trial? If examining a prognosis, was it a longitudinal cohort study? Finally, if studying causation, was it a cohort or case-controlled study?
- Was systematic bias avoided or minimized? Systematic bias is anything that influences the conclusions about groups and distorts comparisons. An accurate test maintains "all else equal," so that the only difference between the groups is the issue being tested.
- Was the assessment "blind"? Those assessing the outcomes need to be unbiased and objective. Even the appearance of conflict should temper assessment of reported results.
- Were preliminary statistical questions addressed? Assessment of a study's reliability: Was there a sufficient sample size? Was the length of the test thoughtfully determined? And was there a complete follow-up?

Finding genetic information via computer-based resources is becoming necessary for obtaining the latest and most accurate data pertaining to any genetic disorder. In order to find relevant information efficiently, it is important to have a general understanding of the topic as well as the method most suitable to the research. Once one determines the best approach to the search, the internet can serve as a valuable resource with up-to-date information that is quickly and easily obtainable.

Paige Hankins is in her second year of the HGP. ■

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From the HAP Director...

By Marsha Hurst

This issue of the *Bulletin* signals an “official” recognition of a new arena for advocacy and a new era for the graduate programs of Health Advocacy and Human Genetics. Each of these graduate master’s programs was the first in its field and both developed out of the needs of patients and families. As a mark of the vision of their founders, both were named with a view toward developing a broad professional scope rather than simply filling that immediate need for direct patient services in hospital settings. The early Health Advocacy Program primarily educated patient representatives, but now it educates a wide range of professionals who advocate for patients, families, communities and healthcare consumers; the Human Genetics Program primarily has educated genetic counselors, but its graduates are now moving into many areas involving research, policy and, yes, advocacy.

The initial focus on a single professional career track—patient representative or genetic counselor—meant that the programs had little to do with each other, despite the fact that they were directed from the same office. (We still marvel at how Joan Marks so capably directed both graduate programs for almost 20 years!) Today, however, as genetic science advances, medical decision making for consumers becomes more complex, psychosocial implications of diseases and disabling conditions require enhanced consumer information, support and advocacy, and barriers to care—incredibly—increase in our society, we recognize the critical arenas in which these programs are becoming conceptually integrated.

Our movement toward creating an integrated “space” between the two programs has been enabled—and, indeed, encouraged—by students and faculty within the programs and faculty in the College. We have written in this *Bulletin* about the few brave and very hard-working students who have pursued joint master’s degrees in Human Genetics and Health Advocacy, and this issue includes a contribution from Meghan Howard, who is currently enrolled in the joint-degree program. As an indication of how much our two programs are already addressing related issues and areas of study, we have three faculty mem-

bers who teach in both programs: Alice Herb in bioethics and research ethics, Sayantani DasGupta in illness narratives and cultural diversity and Mike Smith in research methods and program evaluation.

Within the College, we have been a founding and active part of the Health, Science and Society faculty group, and it is with the intellectual encouragement of this group and the participation of some members of the College faculty that we have really moved our joint advocacy and genetics program forward. During the past year, this intersection has been explored in multiple forums: in Health, Science and Society faculty seminars on “the new genetics”; with Diane Paul, a political scientist from the University of Massachusetts who writes about the history of and policy issues related to genetics and eugenics (see article on page 18); in preliminary work by our two programs and graduate studies on issues related to the protection of human subjects in genetic research and the possible role of an institutional review board at Sarah Lawrence; in last December’s forum on Childhood Asthma in the Community; in an exciting research project on narratives of heritability; and in a Reunion 2004 panel on obesity.

Looking ahead, Rachel Grob has been leading a grant-funded exploration (a Ford Foundation grant through the Council on Graduate Education) of how graduate education in genetics could draw on the curricula and professional models of advocacy to develop professional tracks in two advocacy-related areas, genetics and public health advocacy, and genetics and research ethics. The new SLC Center for Professional Development and Civic Engagement is starting its work with a focus on the health programs and an expansion of our already substantial programming for professionals into more community-based activity, as well as areas in which we can provide professional leadership. The Health Advocacy conference on Advocates in Research, scheduled for January 2005, is planned as the first of a series of forums to bring together advocacy groups from across the spectrum of disease-specific and issue-focused organizations, including genetics, to address critical issues of concern to all health advocates, analyze successful models of



advocacy and forge alliances to work together to promote common goals.

Increasingly, genetics is moving into the public consciousness. Clearly the mapping of the human genome, while mistakenly understood by the public as a completion, is just the beginning of a genuine paradigm shift, moving genetics to a more central place in scientific understanding and ultimately medical practice. As advocates and geneticists, we face a difficult task of promoting the use of this knowledge in a way that acknowledges it is only one factor in a very complicated explanatory system in which environment plays a large and poorly understood role. In addition, we are very aware of the importance of understanding history, lest we be “doomed” to repeat it. This historical perspective on issues of genetics and advocacy stares us in the face with the legacy of suspicion and distrust caused by the Tuskegee study, a constant reminder of how all research embodies the values of society.

Geneticists must become advocates in part because there is a need for public discourse that moves engagement from the world of entertainment and media sensation into the world of thoughtful discussion, evaluation and considered action. As we watch movies like “Twilight of the Gods” and “Gattaca,” read headlines about political battles over stem cell research and cloning, consider the implications of DNA and exoneration of death row inmates, and worry about genetically engineered food and our children’s future, there can be no doubt that genetics and advocacy must be partners in the years ahead. Patients, families, communities, and, indeed, our civic society require this partnership—and SLC is a good place to begin. ■



By Caroline Lieber

In a recent article entitled “Now Can We Talk About Health Care?” (Clinton, 2004), Hillary Rodham Clinton reviews some of the medical advances of the last

From the HGP Director...

100 years and previews some of the changes society can anticipate in the future. Personally, reading articles like this makes me pause and reflect on my 25 years of involvement in the human genetics field. I marvel at the changes in our understanding of molecular genetics that have occurred during the last quarter century.

Over time, genetics, and thus genetic counseling, have become more scientifically complicated. Mendel’s simplistic and straightforward concepts were replaced by new ones with big names like “trinucleotide repeats” and “uniparental disomy.” As a clinician, I eagerly learned these new genetic concepts and developed ways in which to teach them gently to the courageous families with whom I worked, thoughtfully trying to help them gain a sense of control in their out-of-control lives. With great dedica-

tion, we mastered each new concept, our scientific knowledge grew and we moved deeper into the insular, rarefied world of genetic conditions and the scientific literature that explained them.

For the last five years, I have been training others to become genetic counselors. In doing so, I have moved out of the microscopic world of patient care. I have had the opportunity to lift my head up and look around at the place genetics holds at the cross sections of health, science and society. I am ever more persuaded that, as the “burgeoning field of genetics” (Clinton) sprawls outward, the patient-based concerns of genetic counselors will have to broaden as well. The world of genetics is expanding beyond rare disorders and is impacting all people. Diagnosis and management of population-based disorders are taking center stage in health as researchers dissect complex yet common conditions like diabetes and cardiovascular disease, seeking to understand the interaction of genetics and the environment.

Implications of the genetics revolution also impact our lives in areas other than health. As genetics moves into the mainstream, issues such as privacy of information, genetic non-discrimination, protection of human subjects in research and insurance coverage all need to be debated by experts from many fields to determine appropriate policies and equitable use of resources. Our perspectives as genetic counselors need to stretch as well. We need to incorporate the views of policymakers, research organizations, other healthcare professionals, advocacy groups and the lay public, welcoming their contributions to the forthcoming discussions.

I appreciate that there is a great deal of overlap between genetics and health advocacy. Marsha and I have had many discussions about the issues described above. I realize that there is a need to develop a “genetic citizenship” (Jennings, 2003) in which we all take part in raising questions and discussing the myriad issues that likely will affect us as genetics moves into the 21st century. ■

Eugenics, Reprogenetics and Newborn Screening

Continued from page 18

and to make sound decisions regarding pregnancy. In addition, women with PKU who discontinue the PKU diet put their children at additional risk: the mother’s elevated level of phenylalanine crosses the placenta even though the fetus is unlikely to have PKU. Hyperphenylalaninemia affects fetal brain development causing impaired intellectual functioning. Paul’s point is an important one for both genetics and advocacy: even PKU screening, which is in many ways the model for newborn screening pro-

grams, raises a new set of issues. These are, in many cases, issues we are only beginning to understand as the first generation of women with PKU—and possibly other genetic conditions—reaches childbearing age.

Erin Carter is in her second year of the HGP. ■

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Advocates and Genetic Counselors

Continued from page 24

Many in the room seemed to make “saving babies” their sole priority, without fully considering other equally important objectives, such as “saving women” or “providing accurate health information to the public.” It became clear to me on that day that, in order to feel comfortable pursuing the goals of an advocacy organization, the individual advocate must be sure that those objectives do not conflict with her own personal values.

In light of these complexities, I propose that genetic counselors and health advocates begin to consider seriously the

ways in which our two areas of expertise can be integrated to best benefit consumers. Both professions are, by their very nature, concerned about those difficult and controversial issues we confront as we engage in serving individuals, families and the community. Sorting out our own values and their place in our work is central to our integrity as we go forward—and certainly to my own sense of professional ethics and personal principles.

Meghan Howard is a dual-degree student enrolled in both the HAP and HGP. She works as an editorial specialist for the Journal of Andrology. ■

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