Newborn Screening (NBS) and NBS Research

When children are born, their heels are pricked to make bloodspots that are then tested for a variety of disease conditions. In Utah, newborns are screened for 36 diseases, with cystic fibrosis (CF) testing just recently approved. For a test to be considered for inclusion in a NBS program, it must be demonstrated to accurately detect a biomarker or enzyme abnormality associated with disease. An effective NBS program possesses both clinical validity, i.e. the ability to correctly identify future disease risk and clinical utility, i.e. the ability to provide effective treatments to improve the health of those who test positive.

There is a growing appreciation for the research phase of NBS that critically analyzes tests preceding their inclusion in NBS programs. Dr. Wilfond argues that benefit should not be presumed in deciding whether to include new tests because history has shown that this presumptive benefit approach can lead to screening tests that are ineffective or even harmful. Psychological distress due to unclear benefits to screened infants, incomplete understanding of clinical implications, and over diagnosis that results in unnecessary treatment in the screened group illustrate the usefulness of empirical examination. In Utah, the philosophy is that we need epidemiological observational data, preferably in controlled studies, to discover unexpected risks.

Protecting vulnerable research participants is the goal of Institutional Review Boards (IRBs). Informed consent is a cornerstone IRBs use to keep research ethical—a process that informs potential participants about the nature of a research study, its potential risks and benefits, and the voluntary nature of participation. Given this central protective role, it is understandable why IRBs are hesitant to waive informed consent.

It is in the research phase of NBS that Dr. Wilfond argues waiving informed consent is appropriate, “when data support the potential social value and respect..."
tial health benefits of testing and when other safeguards are present. It should be noted that although Dr. Wilfond believes informed consent can be waived for NBS population-based studies, he argues for alternative strategies to increase communication, education, and engagement of parents such as parental education during the prenatal period.

Why ought informed consent be waived in NBS research?

Waivers of informed consent are allowed according to U.S. regulations if four criteria are met: (1) minimal risk, (2) protection of rights and welfare of subjects, (3) research cannot practically be done without a waiver, and (4) participants must be provided additional pertinent information afterward. Dr. Wilfond argues that NBS meets minimal risk standards when research demonstrates that the test has suitable test characteristics and effective therapy is available. Others argue that informed consent could be waived since only bloodspots are used—whether or not there is therapy today—for if these bloodspots could be used for research, there may be therapies for these diseases tomorrow. Dr. Wilfond believes that (2) is met by treating people with respect and consideration of what would be important to them, and (4) could be met with alternate communication strategies. (3) refers to feasibility of study and some believe this point is the strongest support in favor of granting a waiver of informed consent in NBS research.

Logistical difficulty and cost of obtaining informed consent head the list of impediments to obtaining informed consent in NBS population-based research. Many of the conditions screened for are so rare that in a lifetime of medicine a physician may never see a single case. Individualized informed consent as is done now is extremely time and labor intensive. Would a genetic counselor need to explain all tests screened for to everyone despite extremely low probabilities of any one person’s testing positive? Wouldn’t limited time and money be better spent in assessing the information gotten from the bloodspots? Some argue that people could be better informed at a later date—perhaps if they discover that they are at high risk. Others point out that informing after the test has been done begs the question of consent which implies agreement with testing in the first place.

There is no clear definition of minimal risk. Generally, NBS is not creating risk but is informing of risks that already exist. There are three exceptions: We could diagnose (1) some benign conditions as diseases, (2) false negatives, (people erroneously think that they are safe from disease risk), (3) false positives, (people subjected to unnecessary treatment and/or anxiety.) Of these, the risk of false positives is of paramount concern—especially where implications for treatment are ambiguous. We do not know the long term effects of anxiety on people who have been screened and receive false positives, although it is believed that psycho-social risks should be taken seriously.

Two other possible risks from population-based NBS should be mentioned. Potentially, specific ethnic groups could be targeted, although self-reported ethnicity sometimes confuses these results. It also is not clear how we would handle parents who prefer “not to know”, who believe that more information is not always better, especially when discussing such low probabilities. If informed consent were waived, would they opt out of being informed later of their high risk, but be included through the bloodspots in the evaluative NBS research?

Communication

Everyone agreed that we need more education in both routine NBS testing and in NBS research. Ironically, routine NBS does not need to get informed consent but research to evaluate NBS tests does require informed consent. Would we want to have informed consent for all NBS since many people do not know about the NBS tests? Several wondered if the formality of signing a consent form frightens people away from meaningful communication. This arena may be an opportunity for interdisciplinary teamwork—to bring marketers and anthropologists together with scientists and doctors—to increase comprehension, align values, and find better ways of communicating that are alternatives to individualist informed consent.

Dr. Wilfond asked if there might be a system of screening at various ages so as not to overwhelm new parents. The advantage of having all the screening done at birth is the captive audience. What about when later onset diseases are involved? Nicola Longo, MD, PhD, metabolic specialist, emphasized the paramount importance of early detection screening for some of these conditions where serious, irreversible symptoms, such as mental retardation in PKU, are completely avoidable if they are caught before symptoms develop.

Linda S. Carr-Lee

References

2For example, NBS for alpha-1 antitrypsin deficiency in Sweden in the 1970's
3For example, NBS for histidinemia
4For example, NBS of neuroblastoma in Japan in the 1970's
**Physicians Literature and Medicine Program**

*Love in the Time of Cholera*  
June 4, 2008

*Love in the Time of Cholera*, a novel by Nobel-prize winning author, Gabriel Garcia Marquez, chronicles the half-century of love entwining three characters: Florentino, a poet and businessman who has remained unmarried and in love with Fermina, who has had a long, reasonably satisfying marriage to Juvenal, a prominent physician and an illustrious man. After fifty years of unrequited passion, Florentino declares his love once again to Fermina, now a widow. The pair finally become lovers on a boat, cruising up a river without cargo or passengers and flying a yellow plague flag in order to avoid every port and all human contact. In its final pages, this novel explores a great unspoken in our youth-oriented American culture: sexual intimacy between two old people. Well beyond the frantic energies and perilous insecurities of youthful passion, Florentino and Fermina can realize that "they had lived together long enough to know that love was always love, anytime and anyplace, but it was more solid the closer it came to death."

**Evening Ethics Discussion Group**

*“Remodeling the Health Care System: Aspiring Architects and Their Plans”*  
June 12, 2008

We’ve seen more political and public attention to health care this year than at any time since 1993. All of the aspirants to the Presidency have plans, but perhaps more surprising and perhaps more likely to succeed are the plan co-sponsored by Senators Bennett and Wyden and one proposed by another bi-partisan coalition of Senate leaders. All of the plans address cost and access and, to a lesser extent, quality. They differ, of course, in the details, especially with respect to where the responsibility for payment falls, whether the programs are encouraged or mandated and the role of the federal government in the design, construction and operation of the various plans. We’ve attached brief descriptions of the presidential contenders’ plans and a description of the Wyden/Bennett Plan, and the one proposed by Senators Dole, Baker, Daschle and Mitchell. We’ve invited Chamber of Commerce and business leaders, members of the Utah Task Force on Health System Reform, and the State Director and Constituent Liaison staff of Senator Bennett’s Utah office to join us at the Discussion.

Please call the DMEH for articles and address at 408-1135.

**Save the Date!**

Friday October 3rd, 2008

18th Annual Intermountain Medical Ethics Conference  
Guest Lecturers Include:

- Susan Dorr-Goold—University of Michigan  
- Marjorie Ginsburg—Sacramento Healthcare Decisions  
- David Sundwall—Utah Department of Health  
- Allan Ainsworth—Fourth Street Clinic

**Division Members on the Road and in Print**

In May, Leslie Francis attended several meetings including the National Committee on Vital and Health Statistics, the Ethics Committee of the American Society for Reproductive Medicine, and the executive committee of the IVR in Edinburgh, Scotland.

In May, Jeff Botkin published an article in the Hastings Center Report and presented at the NIH Conference on “The Ethical, Legal, and Social Implications of Genetics,” as well as at the Case Western Reserve University Law Medicine Symposium in Cleveland, OH. He also presented at the State University of New York Pediatric Research Ethics Conference in Brooklyn, NY in April.

In May, Armand Antommaria attended the American Academy of Pediatrics’ Committee on Bioethics semiannual meeting.

In April, Jay Jacobson spoke on “Disclosure of medical errors” at the UMA Spring Conference in Springdale, UT. He was honored to receive the Master Award at the 2008 ACP Internal Medicine meeting in Washington D.C. on May 15th. Also in May, he led a panel discussion for Ophthalmology Grand Rounds on “The obligation of caring” and spoke about “Managing our mistakes and those of others” at Orthopedic Grand Rounds at the University of Utah.
Activities and Programs

The Division of Medical Ethics Resident House Staff Conference* will be held at 12:30 p.m. in the UUMC Cartwright Conference Room. The topic is “2008 Advance Directive Update.” The facilitator will be Armand Antommaria.

The Physicians Literature and Medicine Discussion Group* Our facilitator will be Tess Jones. The book will be Love in the Time of Cholera, by Gabriel Garcia Marquez. It will be held in the IMC, Amicus Board Room. Dinner will start at 6:15 p.m. Discussion will begin at 6:30 p.m. Call the DMEH for more information 408-1135.

The Division of Medical Ethics Resident House Staff Conference* will be held at 12:30 p.m. in the IMC Doty Education Bldg, classrooms 3,4,5. The topic is “2008 Advance Directive Update.” The facilitator will be Leslie Francis.

UVR Bioethics Consultation Meeting will meet at 7:00am.

The Division of Medical Ethics Resident House Staff Conference* will be held at 12:30 p.m. in the VAMC Tsagaris Conference Room. The topic is “2008 Advance Directive Update.” The facilitators will be Meg Randle and Deanne Williams.

Our next Evening Ethics Discussion* will meet at 7:00 p.m. Our topic will be "Remodeling the Health Care System: Aspiring Architects and Their Plans" Our facilitator will be Leslie Francis. Please call the DMEH for articles and address at 408-1135.

UUMC Ethics Committee will meet from noon to 1:30 p.m.

UCR Ethics Committee will meet in the Pugh Board Room from 7:30-9:00am.

*These activities are approved for CME credit.

This month’s recommended reading for your enjoyment is by Virginia Woolf:

"On Being Ill"

In her essay, "On Being Ill," Virginia Woolf wonders why illness, a human condition no less universal than "love and battle and jealousy," has seldom served as a theme for the literary imagination. Much has changed since 1930 when Woolf pondered the reasons why writers tended to ignore the poor body and to pursue the exalted mind. Today, we can not only encounter shelves of illness narratives at our local bookstores, but we can also study them as representations of a new distinct literary genre called pathography. While the essay is challenging to read with its meditative and associative style so characteristic of Virginia Woolf, it is a useful reminder about how the world changes and our place in it when we are ill.

You can find this selection by checking our website at www.utahmedicalethics.org, or by calling the DMEH at 408-1135.

CME Statements

Accreditation: The University of Utah School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Designation: The University of Utah School of Medicine designates these educational activities for a maximum of 1 or 1.5 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

ADA: The University of Utah complies with the Americans with Disabilities Act by providing qualified individuals with disabilities access to University programs, services and activities. A request for accommodation can be made by calling (801)408-1135. Reasonable prior notice is required.