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Newborn screenings: Search for standards creates more questions

Ability to test outpaces knowledge of conditions, in some cases

Newborns in every state are screened for disorders that, if undetected, could lead to disability or death; but while some states test for nine or more conditions, others test for only one or two. Now, efforts are being made to bring uniformity to testing nationwide and to determine what tests are the most crucial.

Among the issues being debated are whether tests that show disorders for which there are no treatments should be standard or should merely be available at families' request.

"Over time, states were doing a small number of tests, and then it grew until some were doing eight or nine tests," says **Mary Ann Baily**, PhD, associate for ethics and health policy for The Hastings Center in Garrison, NY. "It turned into somewhat of a patchwork done by the states, and there has been some concern that we see more uniformity and more access."

Several factors determine screens

Because newborn screens, which began in most states with tests for thyroid function and phenylketonuria, have expanded in different states at different rates, there are no national newborn screening standards.

Consensus and uniformity in screening have been affected by state resources available for testing; each state's interpretation of what conditions are treatable and warrant detection; the introduction and availability of new tests; and opinion of the public, legislators, and the medical community.

But the advent of tandem mass spectronomy suddenly meant states with the technology could test for hundreds of conditions — some that are treatable, some that are not, and some that are genetic mutations that geneticists aren't even yet sure cause any problems.

"There are a whole set of disorders that can be identified, and some are lethal and the child will die, while others are not very well understood disorders for which there might be treatments that are untested,"

Baily explains. "So there's a range of these disorders with various implications, but they don't usually meet the standard for screening, which is that we know what [the disorder] is and we know what to do when we find it."

Because technology now allows testing for this broader spectrum of disorders, adding more tests is not difficult. In fact, while some states still test for fewer than 10 disorders, others now are testing for more than 40.

Baily says the quickly expanding possibilities for newborn genetic testing, and the ethical implications of some tests, put pressure on medical policymakers to come up with guidance for standardizing testing.

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Editorial Questions

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Harley Ginsberg, MD, neonatologist at Ochsner Clinic Foundation in New Orleans, says the questions are difficult ones.

"Do you screen for a disease you can't do anything for now?" he asks. "Do families want to know? Also, there's a financial part that can't be ignored. Not every state has the financial wherewithal to pay for these types of screenings, so you screen for the ones where the majority of abnormalities are detected."

Test results only part of picture

Baily says one big factor to consider when putting together a policy on screening newborns is the responsibility that comes when results of those screens are positive.

"Newborn screening is not just a test," she points out. "Screening means follow-up for those that test positive."

Baily says if the more than 4 million babies born in the United States each year are tested for 40 conditions, and several of those tests in each baby return with false positives, there have to be millions of follow-ups for those false positives.

Treatment and long-term follow-up are required for all the newborns whose positive results turn out to be true positives.

In a report released earlier this year, the American College of Medical Genetics (ACMG) recognized that "many states provide the programs necessary to ensure that screening and diagnosis will occur, but are limited in their ability to ensure long-term management, including the provision of the necessary treatment and services."

"It's complicated and expensive," Baily says. "So that's why you have to ask, when you talk about some of these rare conditions that we don't know much about, 'Do I really know there will be a benefit to screening for this?' And that takes evidence."

Ginsberg says delivering positive findings of lesser known conditions to parents carries a responsibility.

"The challenge is that if there is nothing we can do about a disease, then delivering this news to a parent could be a painful, scary endeavor," he explains. "If we are not sure that the abnormality causes clinical disease, then it's even less helpful."

Ginsberg says he would like to see all newborns tested for diseases for which we have accepted, tested treatments, and to let families

(Continued on page 100)

Table. March of Dimes/American College of Medical Genetics Recommended Newborn Screening

The March of Dimes, based upon a report by the American College of Medical Genetics, is urging that all newborns in the United States be screened for 29 disorders for which effective treatment is available. The disorders and their rate of incidence are:

Amino Acid Metabolism Disorders
This is a diverse group of disorders, with varying degrees of severity. Toxic levels of amino acids or ammonia can build up in the body, causing a variety of signs and symptoms, and even death.
PKU — Phenylketonuria >1 in 25,000
MSUD — Maple syrup urine disease <1 in 100,000
HCY — Homocystinuria <1 in 100,000
CIT — Citrullinemia <1 in 100,000
ASA — Argininosuccinic academia <1 in 100,000
TYR I — Tyrosinemia Type I <1 in 100,000

Organic Acid Metabolism Disorders
Without dietary treatment and prevention of acute episodes, these disorders can result in coma and death during the first month of life.
IVA — Isovaleric academia <1 in 100,000
GA I — Glutaric acidemia Type I >1 in 75,000
HMG — Hydroxymethylglutaric aciduria or HMG-CoA lyase deficiency or 3-OH 3-CH3 glutaric aciduria <1 in 100,000
MCD — Multiple carboxylase deficiency <1 in 100,000
MUT — Methylmalonic acidemia due to mutase deficiency >1 in 75,000
Cbl A,B — Methylmalonic acidemia cblA and cblB forms <1 in 100,000
3MCC — 3-Methylcrotonyl-CoA carboxylase deficiency >1 in 75,000
PROP — Propionic academia >1 in 75,000
BKT — Beta-ketothiolase deficiency <1 in 100,000

Fatty Acid Oxidation Disorders
This group of disorders is characterized by inherited defects of enzymes needed to convert fat into energy. Without treatment, the brain and many organs can be affected, sometimes progressing to coma and death.
MCAD — Medium-chain acyl-CoA dehydrogenase deficiency >1 in 25,000
VLCAD — Very long-chain acyl-CoA dehydrogenase deficiency >1 in 75,000
LCHAD — Long-chain 3-OH acyl-CoA dehydrogenase deficiency >1 in 75,000
TFP — Trifunctional protein deficiency <1 in 100,000
CUD — Carnitine uptake defect <1 in 100,000

Hemoglobinopathies
These inherited diseases of red blood cells result in varying degrees of anemia (shortage of red blood cells), serious infections, pain episodes, and damage to vital organs. The severity of these disorders varies greatly from one person to the next.
Hb SS — Sickle cell anemia >1 in 5,000; higher among black Americans (1 in 400)
Hb S/Th — Hb S/Beta-Thalassemia >1 in 50,000
Hb S/C — Hb S/C disease >1 in 25,000

Other Disorders
This mixed group of disorders includes some diseases that are inherited and others that are not genetic. This group of disorders varies greatly in severity, from mild to life-threatening.
CH — Congenital hypothyroidism >1 in 5,000
BIOT — Biotinidase deficiency >1 in 75,000
CAH — Congenital adrenal hyperplasia >1 in 25,000
GALT — Classical galactosemia >1 in 50,000
HEAR — Hearing loss >1 in 5,000; up to 3-4 per 1,000 newborns
CF — Cystic fibrosis >1 in 5,000

Source: American College of Medical Genetics. "Newborn Screening: Toward a Uniform Screening Panel and System," available at www.mchb.hrsa.gov/screening.

decide if they want tests run for less familiar diseases or conditions to which they may be ethnically or genetically prone.

"If the mother's family has the gene for breast cancer, do you test [the baby]?" he asks. "Some families might want to know, and some might not." **(See related story, p. 101.)**

Duane W. Superneau, MD, a geneticist with Genetic Services of Louisiana in Baton Rouge, says even conditions that are not curable have treatments — for example, while there is no treatment for Down syndrome, there are beneficial early interventions.

"That's a common misconception, that there is no treatment," says Superneau. "With many of these conditions, you can maybe employ some therapies that can be helpful down the road, and the earlier you know, the better."

SOURCES

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- **Duane W. Superneau**, MD, Geneticist, Genetic Services of Louisiana, Baton Rouge. E-mail: duane.superneau@womans.org.
- **American College of Medical Genetics**. "Newborn Screening: Toward a Uniform Screening Panel and System," final report, available at www.mchb.hrsa.gov/screening.
- **March of Dimes**, White Plains, NY. Web site: www.marchofdimes.org.
- **The National Newborn Screening and Genetics Resource Center**. Web site: www.genes-r-us.uthscsa.edu.

March of Dimes picks 29

The March of Dimes has endorsed screening all babies for 29 disorders for which effective treatment is available. **(See table, p. 99.)** The recommendation is based on endorsement of the ACMG report, which was commissioned by the U.S. Health Resources and Services Administration, urging screening for these disorders.

The 29 disorders can be grouped into five categories: amino acid metabolism disorders, organic acid metabolism disorders, fatty acid oxidation disorders, hemoglobinopathies, and other disorders.

As of June 1, 2005, 23 states were testing for at least 20 of the 29 disorders recommended in the ACMG report. Fifteen states and the District of Columbia test for fewer than 10.

The March of Dimes also urges states to provide test results for an additional 25 "reportable" conditions named in the ACMG report. There are reliable tests for those conditions, but no documented treatments, yet.

A newborn can't consent to being tested for a genetic condition, so that decision falls to the parents. In the case of disorders for which there is a sure, sometimes lifesaving treatment, Ginsberg says, the choice is clear — the child's health dictates the test should be done.

But when little is known about the condition and even less about how to treat it, or if the genetic markers can only indicate a risk of disease, such as breast cancer, which the child might never develop, should the tests be run and the results disclosed?

"You're drawing blood from a baby, so the decision has been made for the baby," says Ginsberg. "Do you want to know the distant future, even if it might never develop?"

Baily says treatment of some potentially fatal conditions in newborns hinges on early detection, possibly before the conditions and screens can be thoroughly explained to parents, who are presumed to consent to the screenings unless they opt out for religious or other legally permitted reasons.

"There is a strong ethical argument [in medicine] that patients undergoing genetic testing should be able to consent to treatment, but that any 'well-informed newborn' would want to be tested for life-threatening disorders," she says.

But besides parents, who else should — or might — learn of the results of genetic tests?

"It's an issue that we will have to share this information with insurance companies who then may not insure someone who might not even develop the disease," Ginsberg says. "What if you find out you're going to develop Parkinson's disease at age 30 or 40 — do you have to share that with your life or health insurance company?"

Babies and their families may be left in a bind. If they deliberately withhold information about a disorder from an insurance company, they could be guilty of insurance fraud. On the other hand, if they disclose a health condition, they could face higher premiums or complete refusal of coverage.

The effects of that needlestick to the heel, Baily points out, "go far beyond just doing the tests."

"It's very complex, with lots of ethical issues attached." ■

Breast cancer genetic markers: Testing not for all

Arguments for and against screening

Being proactive about health has gained lots of attention from consumers as well as health care providers, and testing for certain risk factors is part of that proactive approach.

But as much as women might want to know their risk of breast cancer, and even though there is lots of information on-line and in print about testing for mutations of the genes BRCA1 and BRCA2 (for BReast CAncer 1 and 2) as indicators of risk for breast cancer, the tests aren't for everyone.

"There are certain women who we recommend should get the information on testing so they can make an informed decision, but there are arguments for and against screening and testing, and it's not real clear cut," says **Debbie Saslow**, PhD, director of breast and cervical cancer control for the American Cancer Society (ACS) in Atlanta.

Family history influences risk

According to the National Cancer Institute (NCI), 5% to 10% of the 192,000 American women diagnosed each year with breast cancer have inherited forms of the disease, some of which are caused by inherited alterations of the BRCA1 and BRCA2 genes. The likelihood that breast and/or ovarian cancer is associated with BRCA1 or BRCA2 is highest in families with a history of multiple cases of breast cancer, cases of both breast and ovarian cancer, one or more family members with two primary cancers (original tumors at different sites), or an Ashkenazi (Eastern European) Jewish background.

However, the ACS and NCI caution that not every woman in such families carries an alteration in BRCA1 or BRCA2, and not every cancer in such families is linked to alterations in these genes.

"We've defined as high risk, women whose close relatives had breast cancer at an early age, or their mother had ovarian cancer, or a male relative had breast cancer, or a relative had bilateral cancer, as factors that would make you very suspicious that something genetic is going on," says Saslow. Adoptions and mostly male families can lessen the historical information a woman has, she notes.

It's a given that some women who have one or more risk factors never get breast cancer, while others with no risk factors do get cancer.

But when is it advisable to recommend to a patient, or support her desire for, genetic testing for genetic mutations?

According to **Jessica B. Mandell**, MS, CGC, a genetic counselor and research coordinator for the New York Breast Cancer Study, which focused on Ashkenazi Jewish women with breast cancer, the first steps are a family history and medical risk assessment, and possibly genetic counseling. Men, too, who have the altered BRCA1 and BRCA2 genes are at greater risk for breast and other forms of cancer.

Cost and how to pay for the testing, which can run hundreds of dollars, is a big issue for some patients. There is controversy over what level of confidentiality a patient can expect, and what will happen if her insurer finds out that there has been a test that could reveal a predisposition to cancer.

If a patient is a candidate and has the testing performed, knowing what to do with the results is the next challenge for her and her physician.

Benefits to positive and negative results

While a negative result brings the relief of knowing that the patient's risk is probably no greater than that of the general population for inherited cancers, even a positive test can carry some benefits.

An individual who receives a positive result is able to take steps to reduce other cancer risk factors, make informed decisions about the future, participate in clinical trials, and ensure proactive health monitoring is kept up so that if cancer does develop, it's caught quickly.

Obviously, the clinician must be attuned to the impact a positive BRCA test will have on the patient's emotions, relationship, and medical choices. Anxiety, depression, and anger are just a few typical reactions. A patient may react by seeking prophylactic mastectomy, for example, before any signs of cancer have arisen. Marriage, childbearing, and other life decisions may be affected.

Negative test results can cause feelings of guilt — for example, in a woman who tests negative for the BRCA gene after her mother and sister have endured cancer. Negative results also can lead to a false sense of reassurance against ever developing cancer.

Positive results can raise issues of privacy and confidentiality, particularly when it comes to insurance coverage.

People covered under employers' group health coverage are protected under the Health Insurance

SOURCES

- **Debbie Saslow**, PhD, Director of Breast and Cervical Cancer Control for the American Cancer Society, Atlanta. Phone: (800) 227-2345.
- **Jessica B. Mandell**, MS, CGC, Genetic Counselor and Research Coordinator for the New York Breast Cancer Study, Sarah Lawrence College. Phone: (732) 651-1094. E-mail: jmandell@slc.edu.
- **National Cancer Institute**, "Genetic testing for BRCA1 and BRCA2: It's your choice." Available on-line at www.cis.nci.nih.gov/fact/3_62.htm.

Portability and Accountability Act (HIPAA) against loss or denial of coverage to someone who does not currently have a disease; however, the protection does not extend to personal insurance coverage, and insurers are not prohibited from asking for genetic background information. Patients who are covered by employers' insurance when the tests are performed and who later leave their employment or otherwise seek new insurance coverage might be denied.

Since 2000, 41 states have enacted legislation related to discrimination in health insurance, and 31 states have adopted laws regarding genetic discrimination in the workplace. However, protections vary from state to state; patients contemplating genetic testing should be advised to seek advice on the laws and protections in their states.

As with screens done on newborns for inborn conditions **(see newborn screening cover story),** someone who deliberately withholds information about a disorder from an insurance company from which he or she is seeking coverage could be guilty of insurance fraud, but disclosure of the information could lead to lost coverage.

Testing children not advised

Saslow says screening children for the BRCA gene mutations is "absolutely not recommended."

"When you do this test, even if the result is positive, it doesn't mean you'll get cancer, and to have that on a 5-year-old would never be recommended," she says. "The average age is still postmenopausal, and most women who have breast cancer catch it early and they survive."

Likewise for genetic testing of unborn baby girls, she says.

"Most people don't feel they would abort a baby with the gene," she says, eliminating the need to test before birth. ■

Return of silicone implants: Safety still center of debate

Panel recommends approval, with restrictions

A Food and Drug Administration (FDA) advisory committee's recommendation that silicone gel breast implants be returned to the United States market after an essential ban of 13 years is being met with approval from some in the medical community and dismay by others.

The FDA must approve the device's return to the market before the silicone gel implants can again be used by most women, but one company, Mentor Corp., has already received an approvable letter, one of several intermediate steps in the FDA review process of new products. Mentor's application to produce what it says are safer, more durable implants received a vote that it is "approvable with condition" in April.

The FDA advisory committee stated in its summary of hearings on the implants that research done by the manufacturer was convincing that only about 1.4% of the implants are likely to break in the first three years after insertion, and that evidence indicated they may last as long as 10 years.

Opponents not convinced

Breaking and leakage of silicone into the users' bodies has been at the center of the silicone implant ban. Women whose silicone breast implants ruptured in the past have attributed myriad complaints to the release of silicone into their bodies, and some research has appeared to support those claims.

Among the complaints attributed to ruptured silicone implants are breast pain, fatigue, muscle and joint pain, hair loss, problems with balance and vision, fibromyalgia, chronic fatigue, autoimmune disorders, migraines, and thyroiditis.

Recognizing the controversial history of silicone implants, in recommending that the FDA approve the implants manufactured by Santa Barbara, CA-based Mentor, the FDA advisory panel set strict conditions for the implants' use, including:

- Patients will sign consent forms acknowledging they understand the risks of implants.
- Mentor only can sell the implants to board-certified plastic surgeons. The surgeons must complete training on inserting the implants.
- Mentor must track how patients tolerate the

implants. They also must conduct formal studies on implant rupture.

• Mentor must warn patients that because implant breaks don't cause immediate symptoms, they should get a magnetic resonance imaging scan five years after implant insertion and every two years after that, and should consider having broken implants removed.

Also, Mentor must establish an independent data safety monitoring committee to periodically review the post-approval data collection and results.

Diana Zuckerman, PhD, president of the National Research Center for Women and Families, who has written that the devices are not proved safe, called the FDA advisors' action "shocking."

Zuckerman cited studies by the FDA that showed "a statistically significant link" between implants and fibromyalgia and several connective tissue diseases.

Following the vote by the FDA advisors, a bipartisan group of female senators led by Sens. Dianne Feinstein (D-CA) and Olympia Snowe (R-ME) urged the FDA to consider women's safety before the agency makes a final decision.

Cosmetic surgeons, who also perform breast implant surgery, have their own complaints about the recommendation. They are fighting the FDA panel's requirement that only board-certified plastic surgeons be permitted to use the silicone implants.

"There haven't been any advances on this issue [since the FDA panel's announcement], but we are continuing to push for the FDA approving the implants so that any qualified cosmetic surgeon can perform this procedure," says **Charlie Baase**, spokesman for the Chicago-based American Academy of Cosmetic Surgery. Cosmetic surgeons argue that board-certified cosmetic surgeons should be considered as qualified to use the implants as board-certified plastic surgeons.

'The time is right' for return

Physicians who practice plastic surgery greeted the potential return of silicone gel implants with praise for the implants and the vetting process that preceded the FDA panel's recommendation.

"The FDA has at last accepted what many of us in the industry have known for some time — silicone implants do not cause disease," says **John A. Grossman**, MD, director of Grossman Plastic Surgery in Denver. "It is true that silicone implants, as with any man-made device, can become worn and break with time, but the material inside is safe."

George Orloff, MD, chief of plastic surgery at Providence Saint Joseph Medical Center in Los Angeles, says the extensive hearings and research that have gone into getting silicone implants back on the market have benefited patients.

"I think the time is right for their return," he says. "The most important thing is this evolution in change based on the process that's been going on a long time. The critical part is that we have heard from a lot of factions — people who are pro-implants, people who are against implants, and people are interested in making sure whatever we do is safe and in the best interest of all involved."

Because of the concerns surrounding possible health risks related to silicone implant leakage, Orloff says silicone breast implants "have become the most investigated of all the implants."

"Board certification and additional physician training as recommended by the panel can only be more beneficial to both patient and physicians," he adds.

Orloff's patients for the last several years, both because of restrictions on silicone implants and concerns over health risks, have asked for saline implants, but the demand is there for silicone, he says.

"Patients' usual preference is for silicone, because it looks and feels more natural," he says. "Now, as more information comes back that can't associate any ill effects due to silicone, and companies are making them safer by using thicker shells and a different formulation of silicone inside, there is a clear demand for silicone."

With the information now available on risks and benefits of silicone implants and the improvements

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- **John Grossman**, MD, President, Grossman Plastic Surgery, Denver. Phone: (303) 320-5566.
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- **Diana Zuckerman**, PhD, President, National Research Center for Women and Families, Washington, DC. Phone: (202) 223-4000.
- **Mentor Corp.**, Santa Barbara, CA. Phone: (800) 525-0245. Web site: www.mentorcorp.com.
- **U.S. Food and Drug Administration**, 5600 Fishers Lane, Rockville, MD 20852. Phone: (301) 827-6500.

in design, Orloff says he would feel comfortable giving the implants to a patient who wants them and is medically appropriate for the surgery.

"And I can't say that about all implants," he says. ■

Direct-to-consumer ads change MD/patient dynamic

Docs say they sometimes feel pressured

You think the patient before you suffering from minor acid reflux will respond just fine to over-the-counter antacids, and you tell her so. But before you ever saw her, she had already decided that that purple pill advertised on television is what she needs, and there's no changing her mind.

It's direct-to-consumer (DTC) advertising at work.

"A lot of times, it's going to fall on the physicians to educate or re-educate their patients, who have seen coverage of medications in the media, whether it's accurate or misleading," points out **Sarah Oetgen**, MPH, senior vice president of SENSEI Health, a media relations and marketing communications firm specializing in health care issues. "It often says a lot about the background of the person who is reading the ads."

Informed drug consumers

Information about prescription drugs was once considered the exclusive domain of physicians, but that changed in 1997 when the U.S. Food and Drug Administration (FDA) lifted its ban against DTC pharmaceutical advertising.

The FDA oversees the advertising of prescription drug products under the federal Food, Drug, and Cosmetic Act and related regulations that aim to ensure that information provided by advertisers is balanced and accurate. Most other advertising, including for over-the-counter drugs, is overseen by the Federal Trade Commission.

According to the Kaiser Family Foundation of Menlo Park, CA, a philanthropy that analyzes and provides information on health care issues, more than 90% of the public reports seeing prescription drug advertisements. Not a surprising finding, considering that pharmaceutical companies spent almost $4 billion in advertising to consumers in 2004, compared to about $250 million a decade ago.

Even critics of heavy DTC advertising, however, concede that well-designed advertising can inform and educate consumers, making them better equipped to make health care decisions. The FDA, in a 2003 report in *FDA Consumer* magazine, said DTC ads "can prompt thoughtful discussions between patients and physicians that result in needed treatments being prescribed."

"DTC ads help educate patients about their health problems, and provide greater awareness of treatments," the FDA reported, citing surveys of physicians and patients and the effects advertising has on them. FDA research demonstrated then that when patients asked about a drug, 88% of the time they had the condition that the drug treated, and 80% of physicians believed patients who ask about a drug understood what condition the drug treats.

Critics counter that DTC ads lead to pressure on physicians to overprescribe unnecessary, expensive, and potentially harmful medications.

Oetgen says DTC advertising "has definitely changed the physician–patient dynamic."

"The whole concept of advertising is to increase awareness, but with direct-to-consumer advertising of drugs, is it making the consumer more aware of the brand name than they are of the side effects?" she says.

Though it has been pressured to endorse limits or bans on DTC ads, the American Medical Association (AMA) has instead called for more study. At its 2005 annual meeting, some AMA delegates had urged an outright moratorium on drug ads, while others suggested any AMA position should come only after more research. Some consumer groups called on the AMA to disclose how much money its *Journal of the American Medical Association* makes on pharmaceutical ads printed in its issues.

The FDA permits three types of advertising of pharmaceuticals to the public:

- product claim advertisements, which include both the product name and specific therapeutic claims;
- reminder advertisements, which provide the name of a product without stating its use;
- help-seeking advertisements, which inform consumers of new but unspecified treatment options for diseases or conditions.

Some critics have said that major pharma companies are spending more on marketing and advertising than on research and development, but according to a 2002 report from the General Accounting Office (GAO), "Prescription Drugs: FDA Oversight of Direct-to-Consumer Advertising

SOURCES

- **Sarah Oetgen**, MPH, Senior Vice President, SENSEI Health, 440 Ninth Ave., 16th Floor, New York, NY 10001. Phone: (212) 631-7779.
- **Kaiser Family Foundation**, Menlo Park, CA. "Impact of Direct-to-Consumer Advertising on Prescription Drug Spending," study available at www.kff.org/rxdrugs/6084-index.cfm.
- **U.S. Food and Drug Administration**, *FDA Consumer*, "The impact of direct-to-consumer advertising," March 2003. Available on-line at www.fda.gov/fdac/features/2003/203_dtc.html.

Has Limitations," industry analyses show spending on research and development in 2001 was more than 10 times the spending on DTC advertising.

"Pharmaceutical companies spent an estimated $30.3 billion on research and development and $19.1 billion on all promotional activities, including $2.7 billion on DTC advertising in 2001," according to the GAO report.

But spending on advertising has grown at a far greater pace than has spending on research and development of new drugs, the GAO said. From 1997 through 2001, spending on DTC increased from $1.1 billion to an estimated $2.7 billion, a growth rate of nearly 250%, while spending on research and development increased from $19.0 billion to an estimated $30.3 billion, a growth rate of 160%. ■

Samples effect residents' drug prescribing habits

Study: Patients might end up spending more

An analysis of the prescribing practices of 29 internal medicine residents in an inner-city Minneapolis clinic indicates that residents with access to sample pharmaceuticals were more likely to prescribe heavily advertised drugs and less likely to prescribe over-the-counter (OTC) drugs than their peers.

The study, reported in the August issue of the *American Journal of Medicine*, was conducted by researchers at the University of Minnesota and Abbott Northwestern Hospital, who recorded the prescribing habits of the residents over a six-month period.

Researchers looked at prescriptions written for highly advertised drugs compared to drugs commonly used for the same indication that were less expensive, available over the counter, or available in generic formulation. By random selection, half of the residents agreed not to use available free drug samples stocked in the clinic by pharmaceutical representatives.

After selecting drug classes where samples of heavily advertised drugs were provided to the clinic, and where lower priced alternative formulations existed, the authors looked for prescribing differences between physicians who had access to free samples and those who agreed before the study to not use the samples.

Author **Richard F. Adair**, MD, wrote that in addition to tendencies toward prescribing heavily advertised drugs, resident physicians with access to drug samples also showed a trend toward less use of inexpensive drugs.

While the initial samples of the drug were free, the authors of the study theorize that the end result would be that because patients tend to develop brand loyalty, patients who were prescribed the more expensive drugs more often than the cheaper or OTC medications stand to spend more over time.

"This could be especially burdensome for low-income patients," Adair wrote.

Cost of 'free' samples questioned

A post hoc analysis considering only drugs commonly used for short-term therapy (nonsteroidal anti-inflammatory drugs [NSAIDs] including cyclooxygenase-2 [COX 2] inhibitors, proton pump inhibitors, and H2 blockers) showed that access to samples of these drugs seemed to be especially influential, associated with less use of inexpensive drugs (63/126, 74/115; $P = .02$), OTC drugs (53/126, 71/115; $P = .002$), and generic drugs (70/126, 80/115; $P = .02$). There was little difference in use of unadvertised drugs (89/126, 87/115).

Access to drug samples influenced prescribing decisions of resident physicians — something that Adair wrote "would seem to violate published national guidelines on physician interactions with the pharmaceutical industry," and furthermore, the physicians observed in the study tended to underestimate their personal response to marketing.

"This finding contradicts two widespread beliefs: Drug samples are inherently different

from other forms of marketing, and samples help patients manage drug costs in the long term," Adair reported.

Researchers conclude that the findings raise questions about whether drug samples should have a place in clinics where residents are learning or low-income patients are receiving care.

"Other studies have shown that many Americans do not take prescribed medications because they cannot afford them," wrote Adair. "Whether to provide 'free' samples of expensive drugs to these patients is an ethical dilemma for many doctors."

For more on the study, see Adair RF, Holmgren LR. Do drug samples influence residents prescribing behavior? A randomized trial. *Am J Med* 2005; 118:881-884. ■

AMA: More pilot studies to boost organ donation

Presumed intent, mandated choice among options

The American Medical Association (AMA) is urging its members to support pilot studies of whether presumed consent and mandated choice policies could increase organ donations, while the nation's organ matching system continues to be skeptical of the success of such programs in the United States.

AMA delegates approved a policy in June seeking more information about presumed intent, in which a person is assumed to be a willing organ donor upon death unless he or she specifically withdraws consent, and mandated choice, which requires people to specifically express their preferences for or against organ donation.

Trustees of the AMA said there currently is not enough data to support a national plan of presumed consent or mandated choice, but that because more than 7,000 patients on the national organ transplantation wait list died in 2004 because of lack of organs, the two methods should be studied to determine if they could be effective in generating more organs for transplant in the United States.

Could 'Spanish model' work here?

Advocates of presumed consent point out that Belgium, Austria, Singapore, the Czech Republic, and most famously, Spain have experienced marked increases in organ donation through use of the presumed consent process.

The AMA's ethics policy addressing presumed consent, adopted in 1993, says presumed consent "raises serious ethical concerns" because to be ethically acceptable, the process should include effective means of documenting and honoring refusals to donate. When there is no documented refusal, AMA ethics canons require the family of the deceased be contacted to verify that they know of no objections to organ donation expressed by the patient before he or she died.

Advocates of presumed consent often cite the "Spanish model" as a successful example of that approach. In one decade, the rate of organ donation in Spain rose more than 145%, topping the rest of the world in the rate of organ donations per million population.

Under Spanish law, organs only can be retrieved after obtaining consent from the family, and the country's national network of specialist physicians who work as hospital transplant coordinators identify potential donors, approach the families, and manage the donors.

Doubt cast on U.S. model

Despite the success of the Spanish model, at least one study casts doubt on how well that approach would work in the United States (Matesanz R. Factors influencing the adaptation of the Spanish model of organ donation. *Transplant International*:Springer-Verlag; 2003), because the part-time physician transplant coordinator, considered to be key to the Spanish program's success, would be difficult to tailor into physician practices in the United States.

At the AMA meeting in June, several black physicians spoke against endorsing presumed consent, saying it could worsen minority distrust of a health care system many Hispanics and blacks believe undervalues them as it is.

AMA trustees indicated more support for mandated choice, in which people would be required to declare their choice when getting a driver's license or other government-issued document.

Other strategies for boosting organ donations that the AMA has expressed interest in are not letting families overrule a dying patient's previously expressed desire to donate and better treatment of hypertension and diabetes patients, to prevent organ failure and thereby reduce the need for transplants. ■

NEWS BRIEFS

Coalition hopes to bridge racial, ethnic gaps in care

Massachusetts General Hospital and Partners HealthCare System have created a center in Boston that will seek to address the deep division existing in medical status between racial and ethnic groups. Mass General and Partners HealthCare have pledged $3 million toward the Disparities Solutions Center. The center will be home to researchers who will seek to bring together health plans, health care providers, and institutions to collect data that show which patients receive what kind of care, and then to use the information to eliminate any disparities that are uncovered.

The Institute of Medicine, in its 2002 report, "Unequal Treatment," found that nationwide, Hispanic and black patients suffer delayed care and higher rates of conditions like heart disease and HIV.

Mass General leaders, in announcing the center, said that after their initial five-year investment they hope that the center will be sustained by grants from foundations and contracts from other hospitals seeking help with disparities projects. ▼

Patient safety act hailed as catalyst for change

The enactment of the Patient Safety and Quality Improvement Act is aimed at enhancing patient safety by encouraging voluntary reporting of errors by providing legal and confidentiality protections to health care providers. The act was backed by a long list of health care associations and patient safety advocates, and passed both houses of Congress with overwhelming bipartisan support.

American Medical Association president **J. Edward Hill**, MD, said in a statement upon the bill's signing that the act "is the catalyst we need to transform the current culture of blame and punishment into one of open communication and prevention."

The legislation creates a reporting system similar to one used by pilots and air traffic controllers who report safety infractions to the Federal Aviation Administration. The bill has been in the works since the groundbreaking Institutes of Medicine "quality chasm" report of 1999, which found that up to 98,000 Americans die each year from medical errors in hospitals.

Under the new law, health care professionals are encouraged to report errors. Patient safety organizations are to be established to analyze the reports, look for weaknesses in the system that may have caused or contributed to the errors, and recommend ways to reduce mistakes. The system is aimed at reducing the number of malpractice lawsuits as well as the number of medical errors. ■

COMING IN FUTURE MONTHS

- New patient safety law: Will it increase reporting of medical errors?
- Getting doctors' attention: How do vendors and drug reps get their feet in the door and around tighter controls?
- Ethics violations: What violations are most often pursued? What penalties result?
- Obese patients: How far should providers push their overweight patients?

Correction

Answers to the CME questions in the **July 2005** issue of *MEA* should have been: **1-D; 2-C; 3-D; 4-A.** ■

CME instructions

Physicians participate in this continuing medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge.

To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity, you must complete the evaluation form provided at the end of each semester and return it in the reply envelope provided to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you. ■

CME Questions

9. The use of mass spectronomy for processing blood samples for genetic testing means:
   A. results are 100% accurate.
   B. labs that once tested for only a few conditions can now easily add hundreds more to the process.
   C. states can easily afford the cost of testing for dozens of conditions.
   D. hospitals will be required to test for 29 conditions suggested by the American College of Medical Genetics.

10. Protections against genetic discrimination in insurance and employment are uniform from one state to the next throughout the United States.
   A. True
   B. False

11. The General Accounting Office, in a 2002 study of pharmaceutical company advertising expenditures, found that, regarding pharmaceutical companies' spending on advertising as compared to spending on research and development:
   A. Companies spent twice as much on advertising as research and development.
   B. Companies spent two times as much on research and development as on advertising.
   C. Companies' expenditures on marketing and advertising grew at a far more rapid rate than did their expenditures on research and development.
   D. Research and development spending grew at a faster rate than marketing and advertising spending.

12. According to at least one study, the Spanish model of presumed consent in organ donations would likely not translate well into the U.S. health care system because:
   A. it relies on part-time physician transplant coordinators, a role that researchers believe does not fit with physician practice in America.
   B. it denies families the right to object to organ donations.
   C. the American Medical Association opposes it.
   D. it costs too much.

Answers: 9-B; 10-B; 11-C; 12-B.