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Dust Devils

VOL. 24, NO. 7

Discover

JULY 2003

SCIENCE, TECHNOLOGY, AND MEDICINE

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Do you want to know your future?

SCIENTISTS UNRAVELED THE BASIC SEQUENCE OF THE 3 billion letters in the DNA of human beings just 37 months ago. When the initial results were announced in June 2000, prognosticators foretold a future in which all diseases would soon be treated genetically. Then more realistic observers noted that not a single attempt to cure any disease using any gene therapy had ever been successful.

In the wake of the hype, one surprising development stands out: People can already get their genome scanned for hundreds and hundreds of diseases. They can discover whether they're more likely than the average person to get cancer, Parkinson's disease, Alzheimer's, diabetes, even a heart attack. It's not cheap yet, but it's getting less expensive with every passing month.

A lot of people will shy away from this opportunity. An interesting case in point is found between the lines of this month's Discover Dialogue, in which author David Ewing Duncan interviews the grandfather of DNA research, James Watson. What isn't revealed in the story is that Duncan has had his DNA sequenced. Duncan says he is a little uneasy about knowing his genetic proclivities, but he believes it was the smart thing to do.

On the other hand, Watson, who started all this, has not had his DNA sequenced. He thinks he may have the Alzheimer's gene, which he suspects runs in his family, but he doesn't want to know unless he can do something about it.

That fear of knowing the future, especially when you're helpless to change it, is also the tension running through Jeff Wheelwright's cover story, which begins on the next page. And it emphasizes a provocative question facing our society at large: Would the United States be a better place to live in if everyone knew his or her genetic future?

Suppose, for example, that the millions and millions of people who will get Alzheimer's disease knew it now. Wouldn't they contribute more to Alzheimer's research? Wouldn't they lobby their congressional representatives to provide more federal funding? Wouldn't many of them volunteer through Alzheimer's aid groups to give overwhelmed caretakers a break? Wouldn't we get a cure sooner?

And wouldn't millions of Parkinson's-prone citizens storm the streets outside the White House the next time President George W. Bush refuses to open up stem cell research? Wouldn't a cure for Parkinson's come sooner?

Information is power, and denial can be deadly. But part of the problem we face is understanding how to interpret DNA tests. No one knows just how well they actually predict the future. The era of genetic testing is still in its infancy. But it will begin with infants.

A nurse rubs alcohol on a baby's foot prior to taking a sample of blood to test for rare genetic diseases, as required by law. The blood samples will be saved and could be analyzed for DNA years later.

Every state in the country requires that infants be tested for a list of obscure diseases. Before long, some states could move on to DNA testing of all newborns. Now is the time to decide a critical question: How much do we want to know and when do we want to know it?

By Jeff Wheelwright
Photography by
Catherine Ledner



TESTING YOUR FUTURE

Austen Muelder was born on August 20, 2002, in a hospital in Santa Barbara, California, a healthy baby in every visible respect. ¶ Shortly after his birth, Austen's mother, Angela, was handed a booklet describing the blood testing that the state wished to perform on her son. California had begun an experimental program to screen newborns for two dozen genetic disorders, a great leap from the four tests required. Angela had no hesitation "if it was going to be for his health." ¶ With a small lancet, a nurse stuck Austen's heel. She held his foot over a card of cotton filter paper while blood dropped onto five circles in a row. When the spots dried, the test was mailed to a state lab in Los Angeles for screening. ¶ Angela and her husband, Jayson, took Austen home to grandmother Linda Fernandez's house in Ojai. Everything was fine for a month. "A perfect baby," Angela remembers. "He had clammy hands and feet, though," says Jayson. "That's kind of odd, we thought, the cold sweats on his feet. He had to wear socks all the time. It didn't seem like anything bad or abnormal, though." ¶ The skin clamminess signaled a serious digestive disorder. Within Austen's system a

metabolic time bomb was ticking, yet for six weeks nobody was able to hear it. Then on the afternoon of October 4, a Friday, his parents got a phone call from the genetics and metabolic disease clinic at the University of California at Los Angeles. Bring your baby to Los Angeles on Monday morning, they were told, and make sure he eats regularly in the meantime. A state laboratory in Berkeley had just flashed the results of the blood test. Austen's life may have been saved by a system known as tandem mass spectrometry.

"Tandem mass spec" is the sharpest new arrow in the quiver of gene testing. Thanks to such technologies, physicians are targeting, managing, and even defeating deadly diseases. The gene screening isn't limited to newborns. Some conditions, like Down's syndrome and spina bifida, are diagnosed in the womb through amniocentesis and more sophisticated probes. At fertilization clinics, for an additional cost, an embryo can be analyzed before it is implanted. Prospective parents who may be carriers of a genetic disorder, such as Tay-Sachs disease or cystic fibrosis, can know for certain by having their own genes tested.

In all these applications, the diseases loom close at hand. But gene tests are beginning to predict long-term illnesses too. Since capturing the sequence of human DNA through the Human Genome Project, scientists have had the "dawning realization," says Wayne Grody, a professor of medical genetics at the UCLA School of Medicine, "that virtually every disease has a genetic component." Researchers even believe that the common maladies of adulthood, such as heart disease and diabetes, have clues within people's genomes, clues that can be found long before the conditions develop. If so, doctors will gain a head start on treatment.

The vanguard for mass predictive testing is newborn screening. These state programs have been running under almost everyone's radar while DNA chips, biotech wizardry, and high-flying personalities get noticed instead. This may be because pharmaceutical companies, which stoke the gene business, seem more interested in adult medicine than childhood disorders.

Without fanfare, new diagnostic methods now screen 4 million babies each year in publicly funded U.S. laboratories. Tandem mass spectrometry, although not as comprehensive as the scans soon to come, can identify more than 30 diseases in a rapid inspection of a spot of blood. Most people don't know it, but gene testing for the masses has already begun.

IN 1958, WHEN AUSTEN'S GRANDMOTHER WAS BORN, BABIES COULD not be tested for genetic disorders. Parents might worry about birth defects, which usually showed themselves at once, but not about inherited conditions gathering to strike an apparently healthy child. Had Linda Fernandez been born a few

years later, her blood would have been screened for phenylketonuria (PKU). You may never have heard of phenylketonuria, but most Americans born since the mid-1960s have been tested for it. Untreated, this genetic condition leads to brain damage and severe mental retardation. Yet it can be readily controlled with a low-protein diet. Thus a simple test can control and even stamp out a rare disease.

By the time Linda Fernandez's son, Jayson, was born in 1981, California was testing for two other conditions—hypothyroidism, an endocrine disorder requiring immediate administration of thyroid hormone so the baby's physical and mental growth won't be stunted, and galactosemia, a metabolic disease that stems from an infant's inability to digest the sugar (galactose) in milk. Unless milk is avoided, the child may die from the buildup of toxic by-products. Newborn screening had cleared Jayson Muelder of three potentially crippling fates.

Before deciding to screen for a disorder, state health departments consider the severity and treatability of the condition, as well as the test's accuracy and cost. During the 1980s, a fourth class of diseases that includes sickle-cell anemia was added to the test panels, or groups of tests. The justification was looser than for the previous three disorders because sickle-cell conditions do not have a decisive therapy. For this reason California was slow to order a sickle-cell test.

It held off until 1990. Five states have still not committed to it.

Now it's a little more than a decade later, and tandem mass spectrometry has brought a sea change in California's newborn screening program. Jayson's son Austen passed the standard battery of four tests within days. It would take a few more weeks to complete the tandem mass spectrometry tests. The basic technique of tandem mass spectrometry is more than a century old, but it was adapted to newborn screening about a decade ago by North Carolina and Pennsylvania. The device, which costs about \$300,000, identifies a range of biochemicals in blood. First, molecules are extracted from the blood sample and converted to a stream of electrically charged ions. The spectrometry is called tandem because the machine analyzes the sample twice in rapid succession, once when the molecules are whole and again after they've been fragmented. The machine sorts the particles by weight, and a computer displays the results as a spectrum of peaks. A peak that is abnormally high or low is the fingerprint of a biochemical disorder. Tandem mass spec is not a DNA test; it searches for genetic flaws the old-fashioned way, by inference. The machine measures the chemical products of the genes, or more often, the lack of a product, which may cause another chemical to peak. Usually the doctor will try to confirm a positive result with newer DNA methodology, going straight to the source of the problem. ▽

After the blood is drawn, a few drops are applied to five spots on a blotter card of cotton fiber. Two spots will be tested; the rest are stored in case retests are needed.

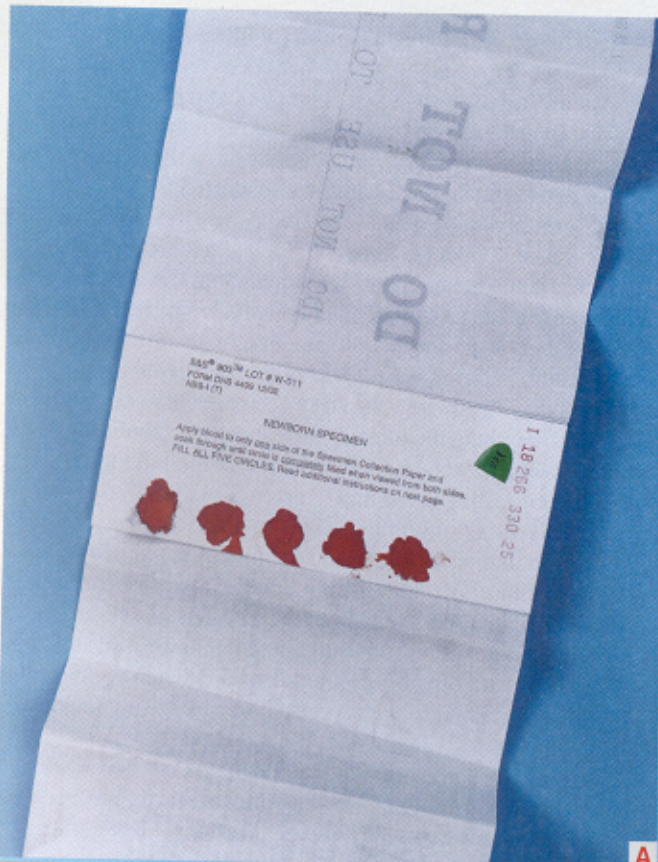
A B

George Cunningham directs California's Genetic Disease Branch laboratory in Berkeley, which monitors procedures for newborn screening in eight labs throughout the state.

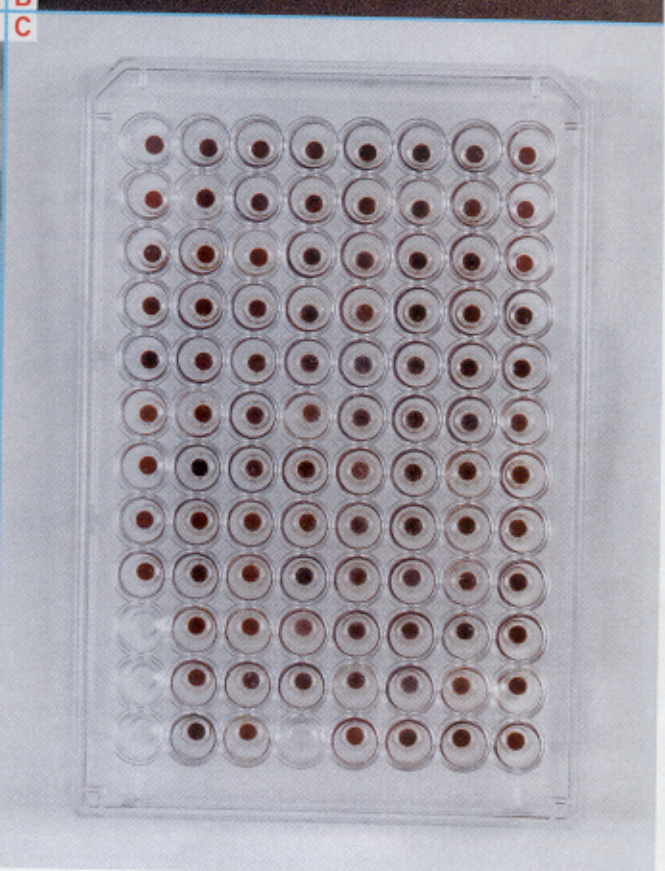
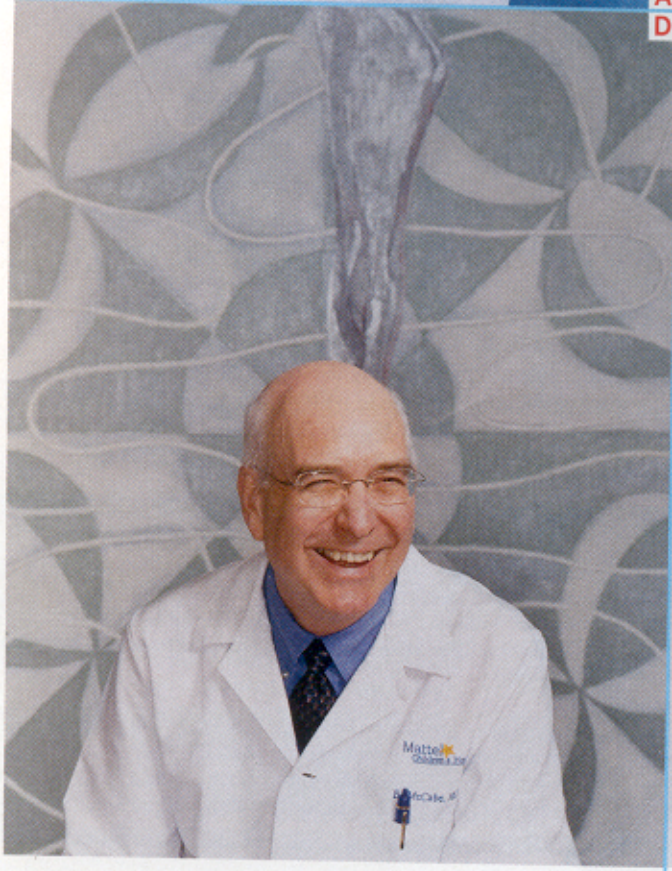
Edward McCabe, chairman of the pediatrics department at UCLA's medical school, is a prominent advocate for the adoption of a national standard for newborn screening programs.

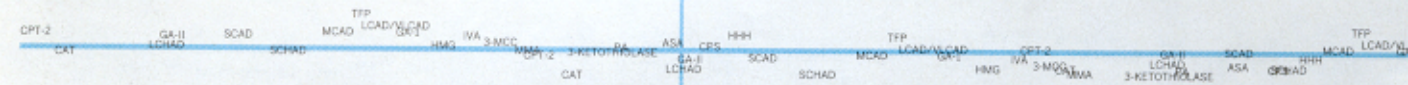
D C

After being specially prepared, the blood spots are mounted in small wells on a tray. Testing an individual well with the spectrometer takes up to three minutes.



A B
D C





In October, a small plastic tray, its top sealed with aluminum foil like a miniature TV dinner, was positioned for analysis in the Berkeley lab. The tray held wells of separate samples from 85 children. One was Austen Muelder's. A thin needle descended from the head of the machine's "auto-sampler" and pierced the foil above one of the samples. A drop of liquid was withdrawn and injected into the machine, where it was gasified, ionized, and analyzed for several dozen of its components. Then the auto-sampler moved to the next sample.

Given the rarity of the conditions under scrutiny, it is a safe statistical bet that 84 of the 85 samples in this particular run produced no unusual spectra. But Austen's readout showed a peak that was 20 times higher than normal for a fatty acid called C-8. A spike at C-8 indicates something called medium-chain acyl-CoA dehydrogenase deficiency, which mercifully can be shortened to the acronym MCADD.

Here is a genetic disease that was unknown, or at least undescribed, a generation ago, although surely it had killed many children before then. MCADD is a recessive disorder. Jayson carries a gene for the condition, and the same flawed DNA is carried by his wife, Angela. Each one is a healthy carrier, but their baby combines the two defective genes.

MCADD refers to an enzyme that helps the body metabolize fat. If it's absent, fatty acids build up in the bloodstream and in the liver. Also, the body is under stress for lack of an energy source. Glucose, a form of sugar, can be drawn on instead of fat, but if glucose is expended because, say, the baby misses one or more feedings, then deadly shock can occur. A baby gets a cold, fusses, won't eat, and the next thing the bewildered parents know is that their child is in a coma. About one-third of undiagnosed children die. Most who don't are severely damaged. Paradoxically, the simple preventive treatment for such a dangerous illness is a regular schedule of feedings with a low-fat formula. If an MCADD child doesn't eat, for whatever reason, the parents know to take

him or her to the emergency room for intravenous glucose. Once Austen's metabolic spike was detected, the response by health authorities was swift. The next morning the Genetic Disease Branch placed phone calls, unsuccessfully, to the Muelders and to their pediatrician. A fax was sent to the pediatrician's office in the afternoon. The state also alerted the clinic for genetics and metabolic disease at UCLA, which was the nearest clinic to the Muelders.

Later that same afternoon, Erica Chang, the nurse coordinator at the UCLA clinic, reached Angela on the phone. She was deliberately vague about the diagnosis until it could be confirmed. "I didn't want to scare them," Chang says.

Stunned, "like being kicked in the teeth," Jayson spent the weekend searching the Internet for information about MCADD. Angela was in tears. Linda Fernandez calmed the young parents by reminding them that "Austen looks perfectly healthy. Obviously, he's not going to die overnight." In fact, the baby was not in danger as long as he continued to eat normally.

By the end of Monday, following workups and counseling at the clinic, Jayson, Angela, and Linda felt reassured about Austen and very grateful for the warning, never mind its lateness. "They find out about other disorders when your baby is in the hospital dying," says Angela. "So I feel really lucky."

CALIFORNIA IS NEITHER THE MOST ADVANCED NOR THE MOST LAGGARD state when it comes to public-health protection, but because it is the most populous, its policies have great clout nationally. The program that caught Austen Muelder's disease is still preliminary: There is no guarantee that tandem mass spec will be made available to all of the 540,000 babies born each year in the state. Tandem mass spec now screens less than half of the babies born in the United States.

Parents' groups and the doctors who treat metabolic disorders have lobbied for expanded newborn testing across the country, and no doubt they would have won their argument by now if the disorders that the new technology detects were more prevalent. "These are stunningly rare diseases," says Michael Watson, executive director of the American College of Medical Genetics. For example, phenylketonuria affects about one infant in 16,000, while MCADD affects about one in 12,000. Galactosemia is even rarer, affecting one in 53,000 infants. A condition called maple syrup urine disorder, which tandem mass spec can flag, has an incidence of about one in 183,000 births.

Detecting Diseases Through Blood

Humans constantly build up and break down molecules during digestion. Tandem mass spectrometry of whole blood can detect major defects in the body's ability to keep all the components of this complex process at healthy levels. The procedure can be used to identify more than 30 metabolic diseases. But tandem mass spectrometry does not detect all diseases. Laboratories must use other types of blood tests to identify diseases such as HIV and sickle-cell anemia.

- Fatty Acid Oxidation Defects (problems with metabolizing fat)** • Carnitine Palmitoyl Transferase Deficiency Type I (CPT-1) • Carnitine Palmitoyl Transferase Deficiency Type II (CPT-2) • Carnitine/Acylcarnitine Translocase Deficiency (CAT) • Long-Chain Hydroxy Acyl-CoA Dehydrogenase Deficiency (LCHAD) • Multiple Acyl-CoA Dehydrogenase Deficiency GA-II • Short-Chain Acyl-CoA Dehydrogenase Deficiency (SCAD) • Short-Chain Hydroxy Acyl-CoA Dehydrogenase Deficiency (SCHAD) • Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCADD) • Trifunctional Protein Deficiency (TFP) • Long/Very-Long-Chain Acyl-CoA Dehydrogenase Deficiency (LCAD/VLCAD) • 2,4 Dienoyl-CoA Reductase Deficiency
- Organic Acidemias (problems with removing waste products)** • Glutaric Aciduria Type I (GA-1) • 3-Hydroxy-3-Methylglutaryl CoA Lyase Deficiency (HMG) •

- Isobutyryl-CoA Dehydrogenase Deficiency • Isovaleric Acidemia (IVA) • Malonic Aciduria • 3-Methylcrotonyl-CoA Carboxyl Deficiency (3-MCC) • Mitochondrial Acetoacetyl-CoA Thiolase Deficiency (3-Kethothiolase) • Propionic Acidemia (PA) • 2-Methylbutyryl-CoA Dehydrogenase Deficiency • Multiple CoA Carboxylase Deficiency • 3-Methylglutaconyl-CoA Hydratase Deficiency
- Amino Acidemias (problems digesting proteins) and Urea Cycle Disorders (problems with ammonia buildup in the blood)**
- Argininemia • Argininosuccinate Lyase Deficiency (ASA) • Carbamoylphosphate Synthetase Deficiency (CPS) • Citrullinemia • Hyperammonemia, Hyperornithinemia, Homocitrullinuria (HHH) • Nonketotic Hyperglycinemia • 5-Oxoprolinuria • Tyrosinemia Type I • Tyrosinemia Type II

However, Watson observes that if you put together all the disorders that are detectable by any available technology, the odds of finding one in any given infant is one in 2,000. Advocates for more screening tend to calculate the prevalence that way in order to fortify their case. Watson is more cautious. He oversees a committee that will recommend national standards for neonatal testing next year. "We will put together scientific criteria for how to evaluate expansion," he says, "and second, we will suggest what disorders should be added." Ultimately, states will decide what tests they can afford and how to fund them. As many critics have noted, today's system is unfair. The states' test panels vary like a patchwork quilt, covering babies in some parts of the country while potentially exposing others to grave illnesses.

The legal rationale for newborn screening is that the state is acting on behalf of children whose health might otherwise be neglected. The ethical argument is straightforward: Early detection can lead to a better outcome. In most states parents can refuse to have their baby tested if they have religious objections, but they are rarely told of that option. For all intents and purposes, the screening for genetic disorders—from as few as three conditions in West Virginia, South Dakota, and Montana to more than 30 in states like North Carolina and Oregon—is mandatory. In the states where consent is necessary for an extra screening by tandem mass spec, parents almost always agree because it doesn't require any additional blood from the infant.

There is a lot more to infant testing than collecting and analyzing blood. Vexing to doctors, the great majority of positive results are false, not because the tandem mass spec or the other assays have made errors but because certain babies are "borderline normal." Their metabolic irregularities don't make them ill. Upon examination, they don't require treatment or further concern. At the other end of the spectrum are infants with grossly abnormal test results, such as Austen Muelder, who need long-term follow-up.

His was one of 12 cases of MCADD detected during the first year of California's experiment with tandem mass spec. As of this May, the project had uncovered a total of 40 metabolic disorders among 331,000 samples, about one in 7,800 cases. When all the results have been reviewed, the governor and the legislature will decide whether to scale up to a permanent program. If so, the cost, which in California has largely been covered by health insurance, would rise from \$60 to about \$80 per screening.

The push to add new tests and to establish a national standard probably won't be decided on the science, although that is strong, says George Cunningham, head of the Genetic Disease Branch of California's Department of Health Services. It will come down to budgetary politics. Cunningham wishes the states had more help. "The federal government has spent billions to characterize the human genome, to develop knowledge that might lead to

testing for genetic disorders in the future, while putting pennies into a program that could benefit children right now," he says.

Three years ago, a task force of the American Academy of Pediatrics published a landmark report titled "Newborn Screening: A Blueprint for the Future." The study said that "newborn screening can lead to early identification and treatment of about a dozen conditions today and perhaps scores of conditions by the year 2010." But it warned, "With these

new technologies comes the ability to detect individuals affected by genetic conditions for which there is no clear advantage to early testing, no early or effective treatment, or no available treatment."

Tandem mass spec is the stalking-horse for more-versatile devices now on the horizon. "Conceivably, we could do 50,000 genetic tests using DNA chips right at the bedside," says Jeffrey Botkin, professor of pediatrics and medical ethics at the University of Utah. "But will the expanded justifications for newborn screening be the wedge for a comprehensive genetic evaluation of children?" he asks. Botkin points out that in addition to long-term health risks, a child's

behavioral traits could be predicted too—the budding elements of personality. How would *that* information be used?

Certainly the reformers of newborn screening don't want to see the program entangled in big speculative questions about genetic medicine. Statements like the following, from an influential paper by Victor McKusick and Leena Peltonen in the journal *Science*, give them a chill: "Currently, newborn babies can be screened for treatable genetic diseases such as phenylketonuria. Perhaps in the not-so-distant future, children at high risk for coronary artery disease will be identified and treated to prevent changes in their vascular walls during adulthood."

What's wrong with that? "Newborn screening has been going on for 40 years," says Trish Mullaley of the National Coalition for PKU & Allied Disorders. "I'd hate to see it lumped together with research into genetic epidemiology. I'm afraid the public won't understand and will be led into thinking screening is a bad thing. People get freaked out about DNA. 'Is this going to end up in some database?' It might make parents say, 'I don't want my child screened.'"

Michele Kling of the March of Dimes adds: "Even if you put it into an informed consent form, we've found that parents would not understand it. You need to act on this information quickly, so for now we'd like every state to start by mandating screening for 10 treatable disorders. Then we'll raise the bar to include others."

Bioethicist Botkin concurs: "If it's not relevant to the child right now, don't do it. Wait until they're adults and let them decide if they want to have these tests." That also was the view of a national committee that looked at the issue in 1997. But Botkin believes that "there will be a change in philosophy eventually" toward screening for conditions that children and their parents

'The federal government has spent billions to characterize the human genome while putting pennies into a program that could benefit children right now'

may not be able to modify. Tests he cites that are currently possible include those for the BRCA1 gene, which indicates susceptibility to breast and ovarian cancer, and HNPCC testing for colon cancer risk. Future tests might provide information about the risk of cardiovascular disease and type II diabetes.

To be sure, no health official is pushing newborn screening in this direction yet, and the means to derive broad diagnoses from an individual's DNA isn't likely to be reliable until Austen Muelder is a teenager. The immediate pressure on health care administrators is whether to look harder for rare but imminent disorders, not for ills whose symptoms may be far off.

One expert with a foot in both camps is UCLA's Edward McCabe. He is executive chairman of the department of pediatrics and physician in chief of Mattel Children's Hospital at the university. When he cochaired the American Academy of Pediatrics task force on neonatal screening a few years ago, he declared himself "a single-issue candidate who will push for a national agenda for newborns." Noting the disparities between the states in testing, he has demanded "equal rights for babies." He's optimistic that a national standard will be adopted. He expects that personal-injury lawyers will prompt it through claims against lax states.

McCabe also directs a think tank that, as he puts it, "explores the tensions surrounding genetics and society." Recently he and his colleagues put on a conference at UCLA that was billed as "the storefront genome" because of its premise that gene scanning will soon be cheap and convenient, providing consumers with unprecedented insights. McCabe has in fact become one of the federal government's top advisers on these matters since the secretary of Health and Human Services tapped him last December to head the department's advisory committee on genetics, health, and society.

So you might say that McCabe is supervising the building of a transcontinental railroad in medical genetics. In one direction he can see the tracks of newborn screening advancing, and in the other direction, starting later but moving faster, the gleaming rails of individual gene testing. At a point in the future the two will come together.

When will that be? McCabe expects that personalized medicine—therapies that address your own cast of genes based on testing—will arrive in 20 to 30 years. "Maybe that's being overly conservative," he adds. "But for the next five to 10 years, the vast majority of genetic testing will be done by newborn screening."

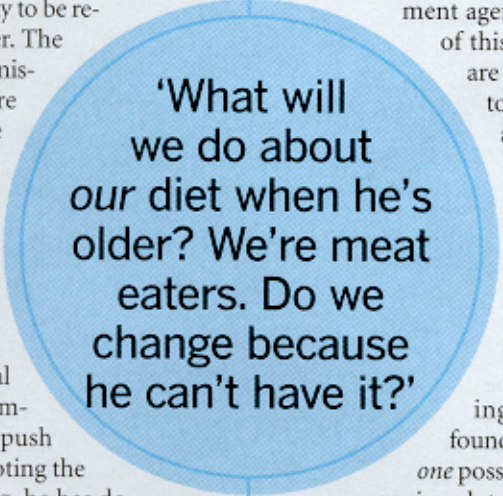
He is therefore enthusiastic about tandem mass spec, although it does not survey human DNA directly. In highlighting metabolic disorders, the process takes a snapshot of what McCabe calls the "metabolome," all the molecules involved in metabolism. He believes more could be done with this system.

And more could be done with millions of people tested in the past. A trove of DNA lies in blood spots from previous

screenings. Most states don't discard their neonatal cards. Several researchers, including McCabe, have shown that genetic information about individuals can be extracted from the spots. (The work has been conducted on "anonymized" samples.)

Newborns aren't the only sources of DNA. McCabe is a wholehearted booster of population screening, and as he points to databases being compiled by military and government agencies, one can easily behold the power of this information. Criminals, for example, are routinely forced to provide their DNA to police and penal authorities. "What if a gene for violence was identified and a treatment was available?" asks McCabe. "A high-risk group would be violent felons. And their DNA is already banked. Would it not be in their own and society's interest to screen for those with the violence mutation who would be amenable to treatment?"

McCabe emphasizes that he is not calling for a national DNA databank to be founded on newborns' or others' records. "It's one possible use," he says carefully. "It's going to require a lot of public dialogue."



EARLY THIS YEAR THE MUELDERS DROVE AUSTEN TO THE GENETICS CLINIC at UCLA for a regular checkup. They brought along the spreadsheets that Jayson had made to record Austen's feedings, and they had a loose-leaf binder with facts about MCADD. Their fears behind them, mother and father were composed and knowledgeable. Their son was a bald-headed bundle of charm, reaching for anyone and anything and trying to stuff whatever he grabbed into his mouth. Grandma Linda cooed and kept him occupied.

The doctor, Stephen Cederbaum, was pleased with the examination. "He'll never be completely free," said Cederbaum, mugging at Austen. "He'll always be on a diet that's free of fat."

"He can't have a Happy Meal at McDonald's," Angela said. "When he's 5, in school, there'll be another set of [dietary] issues to deal with," Cederbaum said. "We'll be seeing this family for a while. We're going to grow together."

Afterward the family went for a bite to eat. Jayson ordered a hamburger, Angela a small pizza, Linda a Reuben sandwich, and Austen had his bottle. The baby formula contained a supplement, carnitine, to assist his digestion.

"The fat has nowhere to go," explained Jayson. "He can't burn it, and it can lodge in his brain."

"What will we do about *our* diet when he's older?" Linda wondered. "We're meat eaters. Do we change because he can't have it?"

That made Jayson think about his own risk for heart disease and how that information might be sifted from his genes decades before the prediction came true.

"He's going to be on a diet that we all should be on anyway," Jayson said. He didn't pick up his burger. Austen, though, reached for it. ☒

Top 10 Causes of Death in the U.S. by Age

DEFINITIONS



Accidents are unintentional injuries, including motor vehicle accidents and medical errors (see below).



Benign neoplasms are tumors that do not spread throughout the body.



Cancer includes all forms of malignant neoplasms (tumors that grow and spread throughout the body).



Cerebrovascular diseases include stroke (damage to the brain by an interruption of its blood supply), atherosclerosis (narrowing of the arteries), and aneurysm (permanent swelling in an artery).



Diabetes mellitus is the more common form of diabetes (the other is diabetes insipidus) and has two types. Insulin-dependent type I is the more severe and usually first appears in people under 35. Non-insulin-dependent type II occurs mainly in people over 40.



Nephritis is inflammation of the kidneys.



Septicemia is blood poisoning.

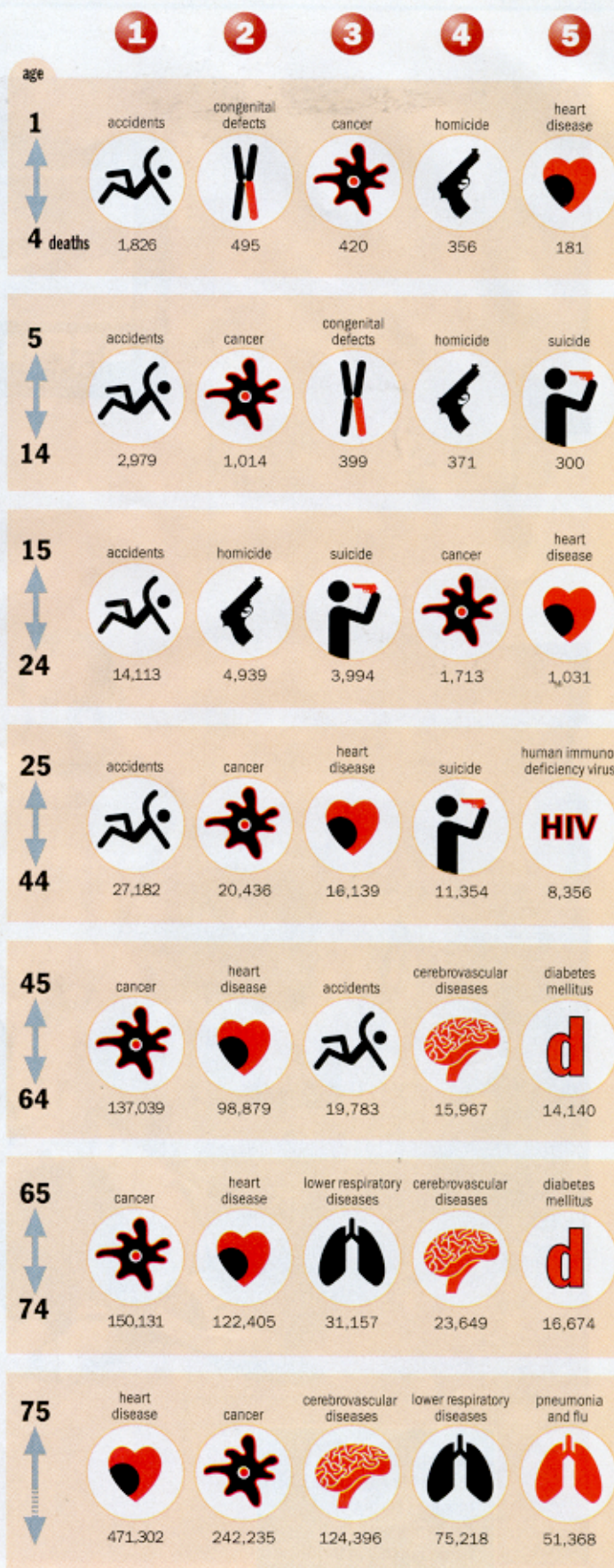


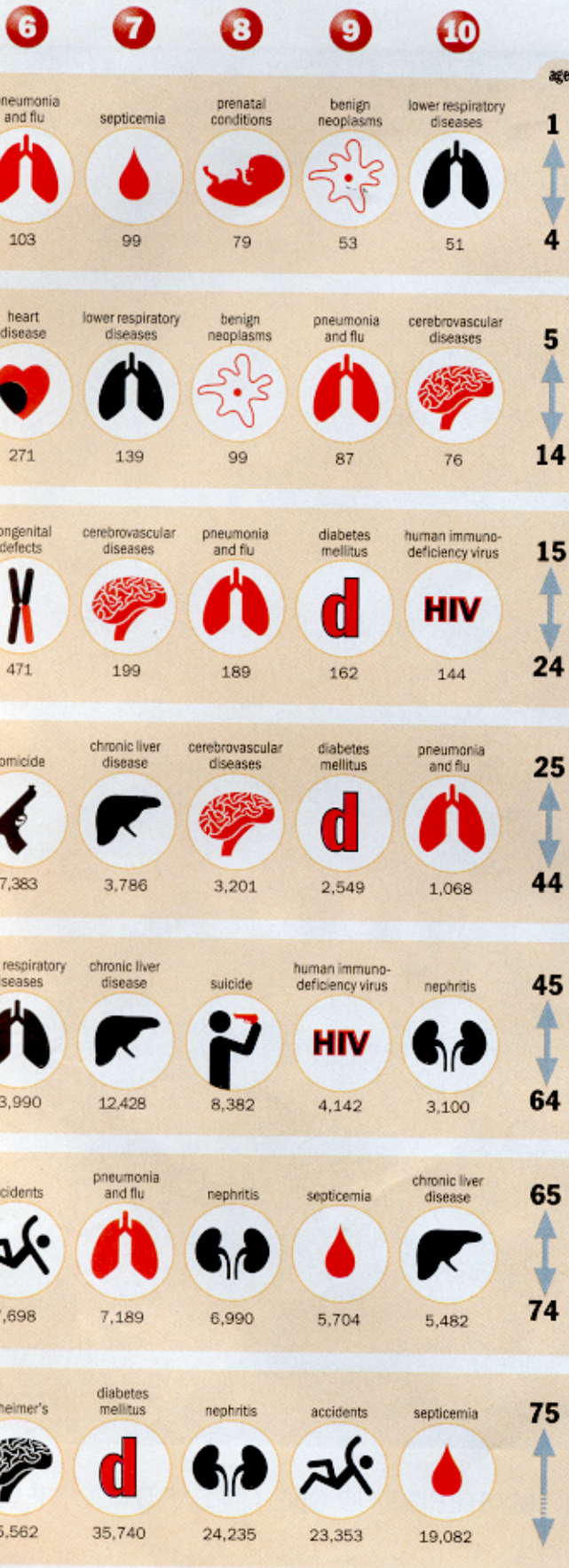
Influenza has surpassed AIDS as a lethal killer and contributes to an average of 36,000 annual deaths in the United States.

Source: Centers for Disease Control and Prevention, 2003

More people die as a result of **medical errors** than from motor vehicle accidents, breast cancer, or AIDS. Reports of the number of error-related deaths vary widely, but some are as high as **180,000 deaths a year**. It is also possible that some deaths due to hospital errors are never reported as such. **Medication errors** alone, occurring either in or out of the hospital, are estimated to account for over **7,000 deaths** in the United States annually.

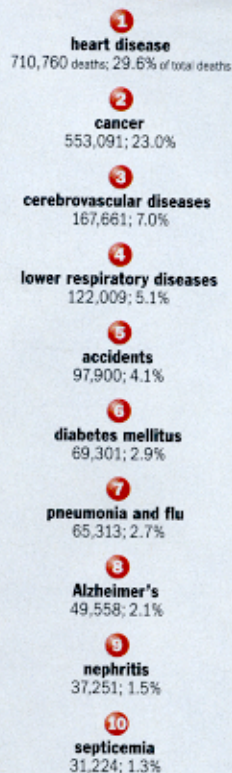
Source: *To Err is Human: Building a Safer Health System*, National Academy Press, 1999





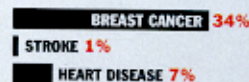
Source for main chart: National Vital Statistics Report, 2002. Numbers are for 2000, all races, both sexes.

Overall, they are:



The diseases people fear most are not necessarily the ones most likely to kill them.

For instance, in a 2000 survey of women age 25 or older, these were what they perceived to be the greatest threats to their health:



...but at the time of the survey, the actual number of annual deaths among U.S. women from these causes were:



Source: Archives of Family Medicine

More to Come

The graphics on this page are from a new book, *Understanding Healthcare*, by Richard Saul Wurman, which will be published in September. From time to time *Discover* will offer readers more pages from the book as they relate to other articles on medicine. Further information can be found at Wurman.com.

