"If you need to be reminded that there are still diseases that can't be cured in an hour—including commercial breaks—then this book is for you. Fantastic stuff."

-HUGH LAURIE
"Lisa Sanders is a paragon of the modern medical detective storyteller. The tales here crackle with suspense. But what sets her apart is her Holmes-like eye for the clues and her un-Holmes-like compassion for those who suffer."


"Dr. Lisa Sanders is the most acute observer of healthcare in America. In this compelling book, she opens the black box of diagnosis and lets us look inside."

- Ian Ayres, author of Super Crunchers: Why Thinking-by-Numbers Is the New Way to Be Smart

"Not 'whodunit' so much as 'whatdunit,'" Lisa Sanders's book brilliantly conveys the sleuthing that lies at the heart of medical diagnosis. But this is more than a set of suspenseful tales unfolded by a skilled storyteller. Amid all the flash and dazzle of the modern doctor's high-tech armamentarium, Dr. Sanders finds that all too often it is the ancient skills, of touch and of attentive listening, that serve the physician, and her patients, best of all. Enlightening for patients, essential for practitioners, this book should be read by every doctor. I'm praying that mine will."

- Geraldine Brooks, author of March, People of the Book, and Nine Parts of Desire

"Lisa Sanders has written a beautiful, thought-provoking book about the sine qua non of medical care-diagnosis. She tells stories about great diagnostic triumphs and explains both the pitfalls and successes of diagnosis. Her patient stories captivate the reader as we try to solve the unfolding mystery. Through these stories we understand and remember the importance of accurate diagnosis."

- Robert Centor, MedRants.com

"Every Patient Tells a Story is a must-read for anyone who has ever been a patient or is a doctor. Written by a physician I respect and a writer I love, the book is filled with intriguing diagnostic dilemmas that will draw you in, and with human stories that will linger in your mind and heart-long after you are done."

- Pauline W. Chen, author of Final Exam
that marks nearly every illness—the diagnosis—revealing the combination of uncertainty and intrigue that doctors face when confronting patients who are sick or dying. Through dramatic stories of patients with baffling symptoms, Sanders portrays the absolute necessity and surprising difficulties of getting the patient's story, the challenges of the physical exam, the pitfalls of doctor-to-doctor communication, the vagaries of tests, and the near calamity of diagnostic errors. In *Every Patient Tells a Story*, Dr. Sanders chronicles the real-life drama of doctors solving these difficult medical mysteries that not only illustrate the art and science of diagnosis, but often save the patients' lives.

LISA SANDERS, M.D., an internist on the faculty of the Yale University School of Medicine, writes the monthly column "Diagnosis" for the *New York Times Magazine* and serves as technical advisor on Fox TV's *House, M.D.* She lives in New Haven, Connecticut.

Also available as an eBook and on audio from Random House
In 1976, Peter Szolovits had a vision of the future. He had a newly minted doctorate in information sciences from Caltech. He was in the vanguard of the computer-savvy. And he had a dream: that joining the data-gathering skills of the physician with the almost limitless memory and data-crunching ability of the computer would allow unprecedented accuracy in the physician's art of diagnosis.

Szolovits came of intellectual age in a time of heady optimism about the capacity of these marvelous inventions. It was the dawn of the modern computer era. Microcomputers were the cutting edge. These computers were the size of a desk rather than the room-sized mainframes that had been the previous state of the art. The personal computer—one that ordinary people could use in their homes—was still just a dream in a Palo Alto garage. Data was still stored on enormous reels of electromagnetic tape. The newly invented LP-sized disk drives were marvels of data storage technology because they could hold 7 megabytes of information.

The rapidly growing ability of computers to store vast amounts of information seemed to fit perfectly with the needs of medicine, in particular the challenges of medical diagnosis. It was obvious that medical knowledge was also growing exponentially. In a 1976 article, a group of doctors working on a computer simulation of "clinical cognition" estimated that a practi-
ing doctor draws on a store of at least two million medical facts. And it was clear that this mountain of knowledge would only grow larger with time. Using a computer "brain" to augment and support human brains in the often bedeviling work of diagnosing illness seemed to Szolovits a logical and technologically feasible goal.

During these heady times Szolovits began a series of conversations with physicians about collaborating to design a computer to help doctors meet the demands of the rapidly expanding universe of medical knowledge. He was surprised by what he found. One conversation in particular with a highly respected senior physician in a university teaching hospital stands out from those days. After listening to Szolovits describe the possibilities of, for instance, entering a set of symptoms into a computer that would then generate a list of likely diagnoses, the physician interrupted him.

"Son," he said, raising his bare hands in front of Szolovits, "these are the hands of a surgeon, not a typist." And he turned on his heel and walked away.

It was an early indication that the application of computers to medical diagnosis might not be as straightforward as Szolovits had thought.

Flash forward thirty years.

By 2006, Szolovits was a full professor at MIT. An energetic man with just the barest hint of middle-aged thickening and a salt-and-pepper beard, Szolovits heads the group at the Massachusetts Institute of Technology devoted to designing computers and systems of artificial intelligence to address problems of medical decision making and diagnosis. Every fall he shares his ideas and insights into this world in a graduate student seminar called Bio-medical Decision Support. I had read about this course and wanted to see what the future of diagnostic software was going to look like.

I visited at the end of the semester, when students presented their final projects. Sitting in a hard plastic chair in the classroom, I watched as PowerPoint slides whizzed by, accompanied by rapid-fire, acronym-studded sentences. One group presented a new technique to look for "interesting hits" amid vast databases; another presented a user-friendly interface for a Web-based electronic medical records program; a third presented a pro-
gram that bolsters the privacy of genetic test data. One group exceeded their fifteen-minute slot to describe an elegant program for identifying potentially harmful interactions between prescription drugs that performs better than the current state-of-the-art software.

All of the projects seemed to improve or expand the boundaries of one or another aspect of health care delivery. Indeed, after the presentations Szolovits chatted with the team who'd created the drug interaction program because not only did it appear to be publishable, it might also be something the students could turn into a business opportunity.

And yet something was missing. Despite the tide of the course, none of the projects addressed the issue that had beckoned so alluringly to Szolovits thirty years ago—the task of improving clinical diagnosis with computers.

In his office after the class, Szolovits leaned back in his chair, musing.

"Thirty years ago we thought we could identify all of the best practices in medicine, create a system that would make diagnosis faster and easier, and bring it all to doctors via a computer," he said. Twenty years ago he wrote a paper for the *Annals of Internal Medicine* that proclaimed artificial intelligence techniques would eventually give the computer a major role as an expert consultant to the physician. And today? Szolovits sighed. "As it turns out, it's simply not possible." It might be an interesting idea, but there's no market for it. Doctors aren't interested in buying it and so companies aren't interested in designing and building it. "Rather than trying to bring the average doctors up to a level of being super-diagnosticians, the emphasis and attention has shifted toward bringing below-average doctors up to current standards and helping even good doctors avoid doing really stupid things. That turns out to provide greater benefits to patients. Plus, there is a financial model for it."

Szolovits ticked off some of the major reasons that most doctors today still rely on their own brains and the brains of their colleagues when making a diagnosis rather than a computerized diagnostic aid.

First, computers can't collect the data from the patients themselves. These machines excel in data crunching, not data collecting. Physicians must collect the data and then enter it into the program. And the program them-
selves don’t make this easy. There are many ways of describing a patient’s symptoms and physical exam findings, but most computers don’t have adequate language skills to understand. You’re left with long pull-down lists of every possible symptom variation or using terms that the computer simply doesn’t recognize.

There are technical difficulties as well. Doctors, laboratories, and hospitals all use different kinds of computer software. No single system can interface with the huge variety of software used to store patient data. Once again the physician must provide the data if she wants it to be considered. Then there are financial difficulties. Who is going to pay the doctor or hospital to invest in this kind of software? Szolovits noted that hospitals don’t get reimbursed for understanding things, they get reimbursed for doing things.

But perhaps the greatest difficulty lies in persuading doctors themselves to use this kind of software. When confronted with a confusing clinical picture, it is often faster and easier for doctors to do what doctors have always done—ask for help from other doctors.

For these and many other reasons, the medical community has yet to embrace any particular computerized diagnostic support system. The dream of a computer system that can "think" better, faster, and more comprehensively than any human doctor has not been realized. For all their limitations, well-trained human beings are still remarkably good at sizing up a problem, rapidly eliminating irrelevant information, and zeroing in on a "good-enough" decision.

This is why human chess players held out for so long against computer opponents whose raw computational and memory abilities were many orders of magnitude better than those of a human brain. Humans devise shortcut strategies for making decisions and drawing conclusions that are simply impossible for computers. Humans are also extraordinarily good at pattern recognition—in chess, skilled players are able to size up the entire board at a glance and develop a feel, an intuition, for potential threats or opportunities.

It took decades and millions of dollars to create a computer that was as good as a human at the game of chess. It is a complex game requiring higher
order thinking but is two-dimensional and based on clear, fixed rules using pieces that never vary. The diagnosis of human beings, in contrast, is four-dimensional (encompassing the three spatial dimensions and the fourth dimension of time), has no invariable rules, and involves "pieces" (bodies), no two of which are exactly the same.

In addition, of course, humans have a set of diagnostic tools that computers may never equal—five independent and exquisitely powerful sense organs. At a glance, a doctor can take in and almost immediately process reams of information about a patient—their posture, skin tone, quality of eye contact, aroma, voice quality, personal hygiene, and hints and clues so subtle they defy verbal description. A computer, in contrast, has only words and numbers, typed in by a human, that inadequately represent a living, breathing, and immensely complicated patient.

Despite the challenges, Szolovits was among those who first attempted to develop computer programs to diagnose medical conditions. Dozens of prototype models were created and tested in a laboratory setting. But most foundered when attempts were made to scale them up, move them into a clinical setting, or make a profit on them. Computers lacked the necessary memory and processing speeds to make vast databases rapidly usable. Until the advent of the World Wide Web, programs had to be distributed via diskettes, or as part of a dedicated computer, or via dial-up modem connections. All of these challenges slowed momentum in the field.

But even systems that have embraced more recent technological improvements have not seen wide success. A case in point is one of the earlier attempts to use computers to improve diagnosis. In 1984 a team of computer scientists from MIT's Laboratory for Computer Science teamed up with a group of doctors from Massachusetts General Hospital, just across the river. They worked for two years to develop an electronic medical reference system and an aid to diagnosis. In 1986 the program, dubbed DXplain, was launched with a database of information on five hundred diseases. National distribution of DXplain with an expanded database of about two thousand
diseases began in 1987 over a precursor to the Internet—a dedicated computer network using dial-up access. Between 1991 and 1996, DXplain was also distributed as a stand-alone version that could be loaded on an individual PC. Since 1996, Internet access to a Web-based version of DXplain has replaced all previous methods of distribution. The program has been continually expanded over the years and is now available to about 35,000 medical personnel, almost all of them in medical schools and teaching hospitals where the program is used as an educational tool.

DXplain and other first-generation diagnostic decision support software programs use compiled knowledge bases of syndromes and diseases with their characteristic symptoms, signs, and laboratory findings. Users enter the data from their own patients by selecting from a menu of choices, and the programs use Bayesian logic or pattern-matching algorithms to suggest diagnostic possibilities.

"There was a lot of work in the 1980s on using computers in diagnostic problem solving and then, in the 1990s, it sort of petered out," says Eta Berner, a professor of Health Informatics at the University of Alabama. Berner may have been part of the reason this work petered out. In 1994 she and a group of thirteen other physicians tested four of the most widely used programs in a paper published in the New England Journal of Medicine. They collected just over one hundred difficult cases from specialists from around the country. They entered the data from each of the patients into each of the four databases. All four programs correctly diagnosed 63 out of the 105 cases included in the study. Overall the four programs provided the correct diagnosis anywhere from 50 to 70 percent of the time—a solid C performance at best.

The authors of the study concluded that the programs tested might be somewhat helpful in clinical settings: "The developers of these systems intend these programs to serve a prompting function, reminding physicians of diagnoses they may not have considered or triggering their thinking about related diagnostic possibilities." But as their study showed, many times the programs would not provide the answers that the doctors are looking for. "The field was sort of a wasteland for a while," Berner explained, but then added, "Now it's picking up again."
One of the difficulties of diagnostic software systems like DXplain is that they try to cover all areas of medicine. Other systems that have been developed as specialized "expert systems" are used by doctors when a case presents a particular type of diagnostic challenge.

Dr. Frank Bia is the medical director of AmeriCares, an international relief organization. He's also a specialist in infectious disease—particularly tropical disease—and until recently a professor of medicine at Yale. He uses a program called GIDEON (Global Infectious Disease and Epidemiology Network) when he sees patients who are sick and have recently returned from other countries. Not long ago he described a case where GIDEON provided clues to a very difficult diagnosis.

It was the early hours of the morning. A twenty-one-year-old woman was moaning softly in her hospital bed. Beside her an IV dripped fluid into her slender arm. Her mother sat next to the bed, her stylish clothes rumpled from her night-long vigil and her face heavy with fatigue.

She'd been brought to the emergency room of this small Connecticut hospital late one night, pale and feverish. "She's been like this for two weeks," the mother told the young physician who entered the room. "And no one can figure out why."

Her daughter had always been very healthy. She'd recently spent a month on a research trip to Africa without any health issues. It wasn't until two weeks after her return to Wesleyan College that she began to feel hot and sweaty. Just standing up made her light-headed. A lengthy nap brought some relief but by the next day, she realized that she was feverish, so she went to the infirmary.

"I told them I thought it might be malaria," the patient explained to the doctor in a barely audible voice. "The teacher told us it was common where we were in Tanzania." And she hadn't always taken the preventative medicine while she was there. The school nurse thought it was probably the Bu. But when the young woman didn't get better over the next several days, the nurse referred her to an infectious disease specialist in town. Maybe it was...
malaria. Since she had been in an area rife with this mosquito-borne illness, the specialist started her on a week of quinine and doxycycline.

She took a full seven-day course, but the medicine didn't help. Over the next few days she developed a cough so violent it made her vomit. She had abdominal pain that made even standing difficult. And she had terrible diarrhea. When she made yet another trip to the infirmary, they called an ambulance to take her to a hospital nearby.

Fadi Hammami, the doctor on duty that morning, listened quietly to the story. He told me later: "I didn't want to miss this diagnosis. She probably had picked up something in Africa; I just had to figure out what it was."

Lying on the stretcher, the patient was thin and pale; her skin was stretched tight across her cheekbones. She had a temperature of 102°. Her blood pressure was low, and her heart was beating fast and hard. She had good bowel sounds, and although her belly was tender, he found nothing else out of the ordinary.

He turned to the lab results sent earlier that morning. Her white blood cell count was elevated, indicating an infection. Some of her white cells were enlarged and their nuclei were irregularly shaped. And something else in her blood work intrigued the doctor: nearly half of her white cells were a single type of infection-fighting cell—eosinophils. Normally these make up only 2 to 7 percent of a person's white cells. In this patient, eosinophils accounted for 41 percent of the white cells in her system. He'd rarely seen that before, and it was an important clue. This type of cell is the body's most effective defense against one class of infectious agents: parasites.

But which parasite? There are dozens, each with a different treatment. Trichinosis, caused by a tiny worm transmitted through infected meat, was capable of this kind of illness. It is rarely seen in this country but is endemic in many African nations. Strongyloides, a parasite that lives in contaminated soil, is also known to cause this type of white cell response, as is filariasis, a disease transmitted by mosquitoes. Which agent was most common in the area of Tanzania she visited?

Dr. Hammami knew he needed help. Dr. Frank Bia provided it. Dr. Hammami had heard of the doctor and called him. He introduced himself and quickly launched into the details of the case. Dr. Bia took notes as he...
listened. He immediately realized that the list of diseases that causes such profound eosinophilia was short. Trichinosis, he told Dr. Hammami, was unlikely because the patient didn't have muscle pain. Filariasis was a much more slowly progressing disease, usually causing symptoms months rather than weeks after the exposure. Strongyloidiasis was a good possibility. So was another disease, schistosomiasis, a parasite carried by snails and transmitted in fresh water. Both infect the gastrointestinal tract and cause diarrhea and both can cause these wild elevations in eosinophils.

But now Dr. Bia hesitated. He was certain that schistosomiasis was found in Tanzania. What about Strongyloides? And was there any other bug that could do this? Even though this was his specialty, Dr. Bia wanted to be certain that he didn't miss anything. Laboratory cultures of blood and stool could probably provide an accurate identification, but that would take days. And this patient was too sick to wait.

Dr. Bia told Dr. Hammami he would get back to him. Hanging up, Dr. Bia turned to his computer and consulted his own ~xpert-GIDEON. It is an expert system created to help physicians diagnose infectious diseases based on their country of exposure. The program recognizes 337 diseases, which are organized by country. Dr. Bia opened the Diagnosis module of the program and entered the information he learned from Dr. Hammami. He also checked out the Epidemiology module for both strongyloidiasis and schistosomiasis parasites, and then the Therapy module to review the best options for treatment. Within ten minutes he had a plan.

"I used GIDEON to be certain I wasn't missing anything," he told me later. "It confirmed my hunch about the best way to proceed."

Dr. Bia called Dr. Hammami back. "Let's just treat her for both parasites," he said. "A two-day course of ivermectin for the strongyloidiasis and a double dose of Praziquantel to knock out the schistosomiasis. And before you start the medicine, send blood and a stool sample to our lab."

Within two days of starting the medications, the vomiting and diarrhea stopped. The fever disappeared. The patient started to eat. She went home
after four days feeling much better, though it would be months before she was completely normal.

The Yale tests showed that the patient had had schistosomiasis. The tiny parasite is carried by a species of East African snail. During heavy rains, snails are washed into rivers, where the parasites disperse. The patient had done some of her research by collecting river water samples. She later admitted that she hadn't worn the protective boots while in the water. They were, she thought, too cumbersome.

Schistosomiasis is such an uncommon disease in the United States that it's not surprising that it was initially missed and the patient misdiagnosed. But the patient might have died before anybody figured it out. Only because Dr. Hammami recognized the significance of the abnormally elevated eosinophils, and consulted an expert in infectious diseases, was the correct treatment found. And, in this case, the expert recognized his own limits and consulted a "digital brain"—an expert system that confirmed his hunches, ruled out other possibilities, and pointed the way to effective therapies.

"I'm not a big high-tech guy," Dr. Bia told me. "But if you don't know about a particular disease or a particular region, you can miss something. This program helps you narrow down the differential. You can look at diseases in certain countries. If someone has a fever and a rash, and they are just back from Ecuador, you can put in the symptoms and the country and it will come up with a list of possible infections."

Expert systems such as GIDEON are used at least occasionally today by specialists such as Dr. Bia. But most general practitioners don't use such systems—or any type of computerized diagnostic decision support. In the case just described, Dr. Hammami—a nonspecialist—recognized the clue in the abnormally elevated eosinophils using nothing but his own hard-won medical knowledge. But what about the nurse and doctor who had seen the patient first? This is precisely the kind of situation in which a never-forgetting digital medical brain would seem to be an ideal tool. If the lab results had been typed into a computer program that was "trained" to watch for
anomalies, an alert might have immediately appeared on the screen, prod-
ding the nurse to consider a parasitic infection and reminding the doctor 
that malaria did not cause a rise in this type of white blood cell.

This, of course, was the vision that had inspired MIT's Peter Szolovirs 
and many others in the 1970s: a computer assistant that was so fast, accu-
rate, and well integrated into the flow of medical information that it would 
save doctors' time and patients' lives. Such a tool does not yet exist. But with 
the rise of the Internet, advances in computer speed and memory capacity, 
and the proliferation of computers throughout the medical system, a second 
generation of diagnostic decision support systems has been developed that, 
if not the Holy Grail, has inspired hope that a more perfect system may yet 
be achieved.

The current paragon of second-generation diagnostic decision support 
systems was, ironically, the result of a near-fatal example of misdiagnosis.

It was early summer, 1999, in suburban London. Three-year-old Isabel 
Maude had a fairly robust case of chickenpox. Her parents, Jason and Char-
lotte, brought her to their family doctor even though they weren't at all 
concerned. After all, chickenpox was an expected childhood rite of passage.
The doctor confirmed the diagnosis and sent them home with the standard 
suggestions for ways to reduce the itching.

But several days after that visit, Isabel developed a high fever, vomiting, 
diarrhea, and severe pain and discoloration of the chickenpox rash. Worried 
now, Jason and Charlotte took Isabel to the emergency room. The doctors 
examined Isabel and reassured them that her symptoms, while more serious 
than normal, were not unheard of for chickenpox. They assured the parents 
that the symptoms would clear within a few days.

The symptoms didn't clear. They got worse. Jason and Charlotte's con-
cern grew into panic. Again they took Isabel to the ER. This time, within a 
few minutes of her arrival, Isabel's blood pressure dropped dramatically and 
she required emergency resuscitation. It was suddenly obvious that Isabel 
was suffering from something a great deal more serious than chickenpox. 
But what? The doctors had no clue. She was rushed to the pediatric inten-
tensive care unit at St. Mary's Hospital in Paddington, London, where Dr. 
Joseph Britto, a pediatric intensive care specialist, took over.
Britto recognized that Isabel was suffering from a rare, but well-described, complication of chickenpox-toxic shock syndrome and necrotizing fasciitis-known in the popular press as the flesh-eating disease. To treat the necrotizing fasciitis, Isabel underwent an emergency operation to remove the infected skin, leaving extensive scars around her stomach and requiring multiple reconstructive operations. Isabel spent two months in the hospital, including a month in the pediatric intensive care unit. She had kidney failure, liver failure, respiratory failure. Several times her heart stopped and she had to be resuscitated. She hovered on the brink of death for weeks.

Slowly, however, she began to recover. The scars from the surgery are today the only physical reminder of her ordeal. As of this writing, she is a bright and active elementary school student.

For Isabel's father, however, the traumatic events were life-changing. The wrenching emotions of watching his child suffer, and the frustration of seeing her condition misdiagnosed, ignited a passion in Jason Maude to do something to improve the system.

At the time, Maude headed equity research in London for AXA Investment Managers, which oversaw $500 billion in investments. He was familiar with using computers to analyze large amounts of complex data. He talked to Britto about the possibility of using computers to improve medical diagnosis. Britto had already been thinking along the same lines, and in July 1999, the pair formed Isabel Healthcare, with the goal of developing a Web-based diagnostic system for physicians.

Britto was convinced that the risks of misdiagnosis could be solved. He likes to compare medicine's attitude toward mistakes with the airline industry's. It was at the insistence of pilots, Britto frequently remarks—who have the ultimate incentive not to mess up—that airlines have studied their errors and nearly eliminated crashes.

"Doctors," Britto often adds, "don't go down with their planes."

The system that Britto helped develop goes considerably beyond the type of expert system represented by GIDEON. Doctors using the diagnostic tool that Britto and Maude named Isabel can enter information using either key findings (like GIDEON) or whole-text entries, such as clinical descriptions that are cut-and-pasted from another program. Isabel also uses a novel search
strategy to identify candidate diagnoses from the clinical findings. The program includes a thesaurus that facilitates recognition of a wide range of terms describing each finding. The program then uses natural language processing and search algorithms to compare these terms to those used in a selected reference library. For internal medicine cases, the library includes six key textbooks and forty-six major journals in general and subspecialty medicine and toxicology. The search domain and results are filtered to take into account the patient's age, sex, geographic location, pregnancy status, and other clinical parameters that are either selected by the clinician or automatically entered if the system is integrated with the clinician's electronic medical record. The system then displays suggested diagnoses, with the order of listing reflecting the degree of matching between the findings selected and the reference materials searched. As in the first-generation systems, more detailed information on each diagnosis can be obtained instantly using links to authoritative texts.

Isabel has had its share of success stories, which the company is understandably proud of. An example occurred not long after Isabel was first available publicly. Dr. John Bergsagel, a soft-spoken oncologist at a children's hospital in north Atlanta, read about the new system and asked to be one of the doctors who would serve as beta testers.

On a weekend day not long afterward, a couple from rural Georgia brought their four-year-old son to the hospital's ER. It wasn't their first visit. Their son had been sick for months, with fevers that just would not go away. The doctors on duty ordered blood tests, which revealed that the boy had leukemia—a type of cancer that attacks cells in the blood. But there were a few things about his condition that didn't add up. For example, the boy had developed these odd light brown spots on his skin around the time these fevers started. No one could figure why these marks appeared but the doctors felt that it wasn't important and scheduled a course of powerful chemotherapy to start on Monday afternoon. Time, after all, is the enemy in leukemia.

When Bergsagel got the case on Monday, it was just one of a pile of new cases. Reviewing the lab results and notes from the examining doctors, Bergsagel was also puzzled by the brown marks, but agreed that the blood test was clear enough—the boy had leukemia. But the inconsistencies in the
boy's case bothered him. He suspected that, although everyone had made note of the rash, the clear diagnosis of leukemia may have drowned out any remaining questions.

"Once you start down one of these clinical pathways," Dr. Bergsagel said, "it's very hard to step off."

But Bergsagel decided to do just that; he decided to give Isabel a shot. He sat down at a computer in a little white room, behind a nurses' station, and entered the boy's symptoms.

Near the top of Isabel's list was a rare form of leukemia that Dr. Bergsagel had never seen before—one that often causes brown skin spots. "It was very much a Eureka moment," he said.

He immediately halted the order to begin massive chemotherapy. The type of leukemia the boy had was particularly deadly and could not be cured or slowed with any of the chemotherapeutic drugs available. Putting the boy and his family through the pain and rigor of chemotherapy would have been excruciating, potentially deadly, and completely pointless. The only possible cure for this form of leukemia was another dangerous option: a bone marrow transplant. The procedure was done, even though the chances of a cure were low. The boy lived another year and a half.

Such anecdotes cannot provide proof of the true utility of Isabel. In order to measure how well the program can perform, two researchers (without any financial or other interests in the system) decided to test the system in cases in a more systematic way.

Mark Graber and a colleague tested the system with fifty case studies drawn from the pages of the New England Journal of Medicine. Since Isabel accepts information two ways, the researchers tested it in both modes. In one, Graber manually typed in three to six key findings from each case study. On average this took less than a minute. The correct diagnosis was included in the list of possible diagnoses generated by Isabel in forty-eight of the fifty cases (96 percent). When the text of entire case studies was cut-and-pasted into Isabel (an artificial, but easy, approach) accuracy declined dramatically, with the correct diagnosis appearing in only thirty-seven of the fifty cases (74 percent).
The authors note that this performance shows that diagnostic decision support systems have evolved significantly since the first-generation systems developed in previous decades. Still, there are many of the same barriers to wide acceptance of the system. Because Isabel and other systems like it are not fully integrated with other medical information systems, data has to be entered into the system by the physician. This is time-consuming and tedious, although Isabel seems to have worked hard to minimize the work involved. Using this system, doctors can describe the patient's symptoms in everyday language. And the machine is smarter, so the amount of detailed information required is much smaller.

But more important, doctors must decide when to use the system. By far the most common diagnostic error in medicine is premature closure—when a physician stops seeking a diagnosis after finding one that explains most or even all the key findings, without asking himself that essential question: what else could this be? If a doctor is satisfied with his diagnosis, he is unlikely to turn to a digital brain at all, and thus the potential value of the system is lost.

So even this new generation of clinical decision-making systems such as Isabel, improved as they are over older programs, is still not widely used. Even Dr. Bergsagel, whose use of Isabel so vividly illustrates that system's power, says he uses it only a few times a month.

"The systems available today are still cumbersome to use," says Jerome Kassirer. "Doctors still have to input all sorts of stuff into these programs... and nobody has the time to type it all in. Besides, most of the time you don't need the system. Most of the day-to-day issues a doctor sees are amenable to the traditional kinds of diagnostic approaches that we've used for years. In fact, it's easier these days because we've got echos and CT scans and MRIs."

One final impediment exists for Isabel and its competitors: price. Isabel is made available to hospitals on a per-bed cost basis, which works out to about $80,000 for a typical hospital. Individual doctors can buy the service for an annual fee of $750.

Although hardly unaffordable by either institutions or individual doc-
tors, the cost of commercial diagnostic decision support systems means that such programs are vulnerable to competition from what might seem like an unlikely quarter: Google.

**Googling a Diagnosis**

Patients, friends, and family have periodically confessed to me that they regularly use Google to investigate their own symptoms. My adolescent daughter does it whenever she is baffled by one of her own body's new and peculiar ways. They are not alone in this. According to a 2005 survey done by the Pew Center, 95 million Americans looked for health information on the Internet. I'll bet that most of those people somewhere along the line in their search used Google.

I got an e-mail several years ago from a reader who had managed to diagnose herself using Google when she developed fever and a rash. She didn't start with Google. She started with a man she had always trusted—her doctor.

"I always heard that when your palms itched it meant you were coming into money," she told her doctor when he entered the exam room. "No money so far," she continued, "but lots of fever." Dr. Davis Sprague eyed her attentively. They'd known each other for years, and despite her playful tone he thought she looked pretty sick.

She'd been well until a few days earlier, she told him. She had a little pain when she went to the bathroom, which made her think she had a urinary tract infection, and so she'd increased her fluids. That didn't work, so the next day she came in and saw a different doctor, who started her on an antibiotic and a painkiller. She didn't get better; in fact, that's when she first noticed the itchy palms. The next morning she was so achy she could barely get out of bed. That night, she had shaking chills and a fever of 102°.

The rash appeared the following day. It started on her arms, her face, and her chest. She stopped taking the painkiller, thinking the rash could be an allergic reaction to it, she told him. But the rash just kept spreading.

Now Sprague was worried. The patient was fifty-seven years old, and
other than a back injury a few years ago and some well-controlled high blood pressure, she had always been healthy. Not today. He was glad she was the last patient of the day because he could tell this was going to take some time.

On examination she looked tired, and her face was flushed and sweaty. Her short, dark hair lay plastered to her scalp. She had no fever, but her blood pressure was quite low, and her heart was beating unnaturally fast. The rash that now covered her body was made up of hundreds of small, flat red marks. The newest ones, those on her legs, were like red-colored freckles. The ones on her arms and chest were larger—the size of nickels—and less well defined. The rash didn't itch or hurt. But the palms of her hands, though rash-free, were red and irritated. A urine sample showed no evidence of an infection, but was positive for blood. That might have been a result of the fever, or it could indicate kidney damage.

"You need to go to the emergency room," Sprague instructed the patient. "You may even need to be admitted to the hospital. I'm not sure what you've got, but I am pretty sure that this is serious."

She might have developed an allergy to one of the medicines she was taking, he explained, which could be dangerous and might even require other medications. What he was really worried about, though, was that she had some sort of infection that was spreading throughout her body. In a hospital they could test her blood and get a better sense of what was going on.

The ER doctor ordered what seemed like an endless stream of blood tests as well as a chest X-ray. When all the tests came back normal, he decided she was well enough to go home. It probably was an allergic reaction, he told her, and gave her a different antibiotic. She should follow up with her doctor in a couple of days, he said.

Two days later, she was back at Sprague's office. She did feel a little better, she said, but she was still having fevers, and now she felt short of breath with even minimal effort. "What do you think is going on?" she asked.

Sprague wasn't sure. Maybe the ER doctor had been right, and it really was an allergy—she was a little better since they'd changed the antibiotics. But the shortness of breath started after that. He was still worried about
fection. Fever and rash were common symptoms. It could be a viral illness—Coxsackie? West Nile? Or was it bacterial? These symptoms, he told her, were so nonspecific that they could be found in everything from garden-variety Lyme disease to something really exotic like Rocky Mountain spotted fever. "We may never figure it out," he confessed. But since she was getting better, he was willing to give her a few more days. If she was still spiking fevers then, he'd send off some blood work to try to find an answer.

At home, though, the patient continued to worry. That night she sat down at the computer to do a little research of her own. "Rash, adult, fever," she Googled.

When you Google a set of symptoms, you don't necessarily get the most common or the most likely diseases; you get the diseases with the greatest number of links from other Web sites. Her Google search brought up dozens of fairly unusual, but well-linked, illnesses: coccidioidomycosis—a fungal infection most common on the West Coast; dengue fever—endemic to the tropics and near tropics; measles; scarlet fever.

But the patient immediately focused on the first result: Rocky Mountain spotted fever, which her doctor had mentioned. As she read about the disease, she began to feel a little panicky. The description of the symptoms, she said, fit her perfectly: the rash, the fever, the muscle aches. The rash, she read, can involve the palms of the hands, which is pretty unusual. She didn't have a rash there, but her palms were red and itchy. Also, the disease is transmitted by dog ticks—she had a dog. It's most common in the summer—it was August. Though it's rare, it is more commonly seen on the East Coast than in the Rockies, and she was in upstate New York. People can die from this disease, she read. It's the deadliest of all the tick-borne illnesses.

She called the emergency room where she had been seen. Had they tested her for Rocky Mountain spotted fever? No, she was told, why would they? They had never seen a single case in the area. She hung up feeling somewhat relieved. They didn't think it was Rocky Mountain spotted fever; Dr. Sprague didn't think it was. Chances are that it wasn't.

Over the next few days, the patient started to feel almost normal again. The rash was fading—though now it itched like crazy—and her energy was
coming back. But she continued to have fevers at night and still occasionally felt short of breath. She returned to Sprague's office one more time. "I'm glad to hear you're feeling better, but these fevers worry me," he said. "I want to send off some tests."

"What about Rocky Mountain spotted fever?" the patient asked. She confessed that she had looked it up on the Internet and thought the symptoms were close to what she had. The doctor thought for a moment. "I don't think that's what you have, but let's add it." He had heard doctors complain about their patients surfing the Web for diagnoses, but he didn't mind. He had never seen Rocky Mountain spotted fever—maybe she was right.

The results came back a few days later. "You're an internist's dream," the doctor said with a smile as he entered the exam room. "It really is Rocky Mountain spotted fever, and I would have completely missed it if I hadn't listened to you." He started the patient on doxycycline—the antibiotic of choice for this bacterium. Her body seemed to be fighting off the illness without it, but he wasn't taking any chances. Within a few days her fever was gone, the rash was fading, and her palms were beginning to feel normal.

I asked the patient how she felt about her doctor, who had come so close to missing this diagnosis. "But he didn't miss it. He was the first to think of it. And he sent off the test—even though it could prove him wrong. He just wanted to figure out what was going on."

This case illustrates a real and growing trend—patients who either diagnose themselves by using the Internet or follow up on their doctor's diagnosis in that manner. But it's not just patients using the power of Google and other search engines these days. A doctor wrote to the New England Journal of Medicine about an amazing diagnosis made at his institution. The case involved an infant with diarrhea, an unusual rash, and multiple immunological abnormalities. The patient was discussed at length in a case conference with residents, attending physicians, and a visiting professor. No consensus was reached. The letter continues:

Finally, the visiting professor asked the fellow if she had made a diagnosis, and she reported that she had indeed and mentioned
a rare syndrome known as IPEX (immunodeficiency, polyendocrinopathy, enteropathy, X-linked). It appeared to fit the case, and everyone seemed satisfied ...

"How did you make that diagnosis?" asked the professor. Came the reply, "Well, I had the skin biopsy report, and I had a chart of the immunologic tests. So I entered the salient features into Google, and it popped right up."

This story and their own experiences with patients who had consulted the Internet for information about their own symptoms prompted a pair of Australian researchers to test Google's diagnostic accuracy.

Like Graber, they used the medical case studies published in the New England Journal of Medicine, selecting three to five keywords from each article, and entered them into Google before they, themselves, read the actual diagnosis. The doctors selected and recorded the three most prominent diagnoses that Google came up with for each case. Then they compared the Google findings with the real diagnosis.

The result? Google flunked. Google found the right diagnosis for only fifteen out of twenty-six cases (58 percent). Of course, Google isn't designed to provide diagnostic support for doctors, so any right answers provided by the powerful search engine are bonuses. One interesting observation was made by the authors: Google was most accurate for diseases that had unique signs and symptoms or rare presentations. This isn't surprising to any of us who use Google, but it's interesting. As anybody who has used a search engine knows, the more unusual your target is, the easier it is to find. For example, if you want to Google two friends, you are much more likely to find the one named Ionia Khammouane than the one named Ann Jones. Information on Ionia is going to pop right up, just like the diagnosis of the case of the child with leukemia and the brown marked rash.

What's interesting is that it's precisely the unusual disorders—the ones with peculiar symptoms that doctors rarely see—that can be most baffling to both doctors and patients. In the case I presented in an earlier chapter, a resident in our program was able to diagnose a patient with intermittent
nausea and vomiting because of an unusual symptom—her nausea was improved by hot showers. By Googling that, Amy Hsia was able to identify an unusual and recently described disease called cannabinoid hyperemesis.

Because Google is so universally available, simple, fast, and free, it may become the go-to diagnostic aid for oddball cases. Even the august *New England Journal of Medicine* finds Google "helpful in diagnosing difficult and rare cases." Google gives users ready access to more than three billion articles on the Web and is far more frequently used than PubMed for retrieving medical articles.

The authors of the Google study note that, in fact, Google is likely to be a more precise diagnostic tool for clinicians than the lay public because clinicians will use more specific search terms ("myocardial infarction" rather than "heart attack," for example) and will be better able to identify likely hits because of their preexisting knowledge. Patients, using everyday language, are likely to end up with fewer useful hits buried in pages of irrelevant sites. Their ability to distinguish the useful hits will be compromised by their unfamiliarity with medical language.

The power of Google in the realm of medical diagnosis has not been lost on Google itself. Google has formed a Health Advisory Panel to inform its work in this area. And Google has launched a major effort to improve the quality of medical-related searches by having reputable organizations (such as the National Library of Medicine) and individual doctors flag Internet sites offering reliable information. These sites are then given prominence when search results are returned and are labeled with the individual or organization that has vetted them.

Google is very open about its plans to improve search capabilities for patients, but the company is mum on the subject of doing the same thing for physicians (Google representatives declined to be interviewed on this subject). Perhaps that's because doctors are a valuable audience and if Google can find a way to improve diagnostic search results to the point of being more accurate than Isabel and other commercial systems, it could effectively capture the market and be able to leverage all those physician "eyeballs" with advertisers.

But even a more accurate Google-based diagnostic decision support sys-
tem wouldn't really solve the problem of missed diagnoses. To begin with, any system that must be consulted separately from the digital workspace in which a doctor or nurse deals with a patient will only be used when there is uncertainty in the mind of the health care professional. If a doctor is sure of her diagnosis, or a nurse is certain that the correct medication has been prescribed, they won't turn to Google (or Isabel, or DXplain, or any other system).

Computer programs won't really make a dent in the problem of misdiagnoses and other types of medical errors until they are much "smarter" and easier to use than they are today.

"Future systems need to operate in the background," says Eta Berner, the researcher who has tracked progress in medical computing for decades. "The doctor shouldn't have to enter anything. The system should be able to extract information from what the doctor or nurse is already doing ... taking notes or entering lab values or prescribing medications. The system should be intelligent enough to provide an alert or a reminder only if something is really missing ... a test, for example, or a medication."

Berner foresees a time when all of the now fragmented information streams in the health system will be unified and made consistent. Patients' health records will be fully digital— including images such as MRI scans or X-rays. Standard words, phrases, and units of measurement or description will be used so that computer systems in distant locations can intelligently and accurately use the information. Doctors and nurses will enter all information in digital form—handwriting (never doctors' strong suit anyway) will be obsolete.

With this kind of a system in place, the possibility of infection with the schistosomiasis parasite would have popped up the very first time the young woman described earlier was evaluated in an emergency room. The likelihood that little Isabel Maude was suffering from a rare complication of chickenpox would not have been easy to ignore. And the patient with Rocky Mountain spotted fever wouldn't have had to use Google herself ... her doctor would have already seen the tight fit between her symptoms and that possible diagnosis.

Of course it will be years—and more likely decades—before this kind
of a system is in place. And although I think it is inevitable that the vast resources of the digital age will become more fully integrated into our health care system and the doctor's diagnostic routine, it may not take the form we anticipate. Computers have already revolutionized our diagnostic abilities dramatically. I think the first and most important digital diagnostic tool developed was the CT scanner. It was the development of powerful computers that allowed us to capture data from a series of two-dimensional images to create a three-dimensional representation of the body. Since 1972, when the CT scan was first developed, this tool has made routine diagnoses that would previously only have been discovered after death. So while we envision a future where the computer learns how to think like a doctor, it is possible that its greatest contributions will take a very different form.

Would a kind of super-efficient, integrated, intelligent computer system eliminate all diagnostic challenges? Would it replace doctors? Hardly. I believe the process of diagnosis will be made more effective and that it will be faster and easier in the future to zero in on what's really wrong with a patient. But there will always be choices to make-between possible diagnoses, between tests to order, and between treatment options. Only a skilled and knowledgeable human can make those kinds of decisions.

And, of course, people need more than the right treatment for the right disorder. They need to be heard, they need assurance, explanations, encouragement, empathy—the full range of emotional support that is a critical part of what we doctors try to do: heal.