

INTRODUCTION

Every Patient's Nightmare

Barbara Lessing stared out the window at the snowy field behind the hospital. The afternoon sky was dark with yet more snow to come. She looked at the slender figure in the bed. Her daughter, Crystal, barely twenty-two years old and healthy her entire life, was now—somehow—dying. The young woman had been in the Nassau University Medical Center ICU for two days; she'd been seen by a dozen doctors and had scores of tests, yet no one seemed to have the slightest idea of just what was killing her.

It all started at the dentist's office. Crystal had had a couple of impacted wisdom teeth taken out the month before. But even after the teeth were gone, the pain persisted. She'd called her mother halfway across the state just about every day to complain. "Call your dentist," she'd urged her daughter. And she had. Finally.

The dentist gave her a week's worth of antibiotics and then another. After that her mouth felt better—but she didn't. She was tired. Achy. For the next week she'd felt like she was coming down with something. Then the bloody diarrhea started. And then the fevers. Why didn't you go to the doctor sooner? the trim middle-aged woman scolded her daughter silently.

Barbara had gotten a call from a doctor in the emergency room of this suburban hospital the night before. Her daughter was ill, he told her. Deathly ill. She drove to Syracuse, caught the next flight to New York City,

and drove to the sprawling academic medical center on Long Island. In the ICU, Dr. Daniel Wagoner, a resident in his second year of training, ushered her in to see her daughter. Crystal was asleep, her dark curly hair a tangled mat on the pillow. And she looked very thin. But most terrifying of all—she was yellow. Highlighter yellow.

Wagoner could feel his heart racing as he stood looking at this jaundiced wisp of a girl lying motionless on the bed. The bright unnatural yellow of her skin was shiny with sweat. She had a fever of nearly 103°. Her pulse was rapid but barely palpable and she was breathing much faster than normal despite the oxygen piped into her nose. She slept most of the time now and when awake she was often confused about where she was and how she had gotten there.

To a doctor, nothing is more terrifying than a patient who is dying before your eyes. Death is part of the regular routine of the ICU. It can be a welcome relief to the patient, or to his family. Even a doctor may accept it for a patient whose life can be prolonged no longer. But not for a young girl who was healthy just weeks ago. These doctors had done everything they could think of but still there was a fear—a reasonable fear—that they'd missed some clue that could mean the difference between life and death for this young woman. She shouldn't die, but the young resident and all the doctors caring for her knew that she might.

Crystal's thin chart was filled with numbers that testified to how very ill she was. Wagoner had been through the chart a dozen times. Virtually every test they'd run was abnormal. Her white blood cell count was very high, suggesting an infection. And her red blood cell count was low—she had barely half the amount of blood she should have. She'd gotten a transfusion in the emergency room and another after she was moved to the ICU, but her blood count never budged. Her kidneys weren't working. Her clotting system wasn't either. Her yellow skin was covered in bruises and her urine was stained deep red.

Sometimes, if you just work hard enough to keep a patient alive—to

keep the blood circulating, the lungs oxygenating, the blood pressure high enough—the body will be able to survive even a vicious illness. These are the miracles brought by technological advances. Sometimes, but not this time. The ICU team gave Crystal bag after bag of blood; they did their best to shore up her damaged clotting system; she got pressers (medications designed to increase blood pressure) and fluids to help her kidneys. She was on several broad-spectrum antibiotics. And yet none of that was enough. She needed a diagnosis. Indeed, she was dying for a diagnosis.

This book is about the process of making that diagnosis, making any diagnosis. So often this crucial linchpin of medicine goes unnoticed and undescribed, yet it is often the most difficult and most important component of what physicians do. As pervasive as medicine has become in modern life, this process remains mostly hidden, often misunderstood, and sometimes mistrusted. In movies and novels it's usually the one-liner that separates the fascinating symptoms from the initiation of the life-saving therapy. On television it's the contemporary version of Dr. McCoy's (*Star Trek*) magic diagnostic device (his tricorder) that sees all, tells all. But in real life, the story of making a diagnosis is the most complex and exciting story that doctors tell.

And these are stories that doctors tell. Just as Sherlock Holmes or Nick Charles (the hero of the *Thin Man* mysteries) or Gil Grissom (*CSI*) delights in explaining the crime to victims and colleagues, doctors take pleasure in recounting the completed story of their complex diagnoses, stories where every strange symptom and unexpected finding, every mystifying twist and nearly overlooked clue, finally fit together just right and the diagnosis is revealed. In this book I'll take you into those conversations and onto the front lines where these modern medical mysteries are solved—or sometimes not.

Just a hundred years ago, journalist and acerbic social critic Ambrose Bierce defined the word “diagnosis” in his *Devil's Dictionary* as “A physician's forecast of disease by [taking] the patient's pulse and purse.” And that was true

for most of human history. Until very recently, diagnosis was much more art than science.

But since Ambrose Bierce wielded his rapier pen, there has been a revolution in our ability to identify the cause of symptoms and understand the pathology behind them. In the era in which Bierce wrote, Sir William Osler, considered by many to be the father of American medicine, was able to write a comprehensive summary of all the known diseases in his 1,100-page masterwork, *The Principles and Practice of Medicine*. These days each tiny sub-branch of medicine could provide as many pages on its super-specialized knowledge alone.

At the birth of medicine, millennia ago, diagnosis (the identification of the patient's disease) and prognosis (the understanding of the disease's likely course and outcome) were the most effective tools a doctor brought to the patient's bedside. But beyond that, little could be done to either confirm a diagnosis or alter the course of the disease. Because of this impotence in the face of illness, the consequences of an incorrect diagnosis were minimal. The true cause of the illness was often buried with the patient.

In more recent history, medicine has developed technologies that have transformed our ability to identify and then treat disease. The physical exam—invented primarily in the nineteenth century—was the starting point. The indirect evidence provided by touching, listening to, and seeing the body hinted at the disease hidden under the skin. Then the X-ray, developed at the start of the twentieth century, gave doctors the power to see what they had previously only imagined. That first look through the skin, into the inner structures of the living body, laid the groundwork for the computerized axial tomography (CT) scan in the 1970s and magnetic resonance imaging (MRI) in the 1990s. Blood tests have exploded in number and accuracy, providing doctors with tools to help make a definitive diagnosis in an entire alphabet of diseases from anemias to zoonoses.

Better diagnosis led to better therapies. For centuries, physicians had little more than compassion with which to help patients through their illnesses. The development of the randomized controlled trial and other statistical tools made it possible to distinguish between therapies that worked and

those that had little to offer beyond the body's own recuperative powers. Medicine entered the twenty-first century stocked with a pharmacopeia of potent and effective tools to treat a broad range of diseases.

Much of the research of the past few decades has examined which therapies to use and how to use them. Which medication, what dose, for how long? Which procedure? What's the benefit? These are all questions commonly asked and that can now be regularly and reliably answered. Treatment guidelines for many diseases are published, available, and regularly used. And despite concerns and lamentations about "cookbook medicine," these guidelines, based on a rapidly growing foundation of evidence, have saved lives. These forms of evidence-based medicine allow patients to benefit from the thoughtful application of what's been shown to be the most effective therapy.

But effective therapy depends on accurate diagnosis. We now have at our disposal a wide range of tools—new and old—with which we might now make a timely and accurate diagnosis. And as treatment becomes more standardized, the most complex and important decision making will take place at the level of the diagnosis.

Often the diagnosis is straightforward. The patient's story and exam suggest a likely suspect and the technology of diagnosis rapidly confirms the hunch. An elderly man with a fever and a cough has an X-ray revealing a raging pneumonia. A man in his fifties has chest pain that radiates down his left arm and up to his jaw, and an EKG (electrocardiogram) or blood test bears out the suspicion that he is having a heart attack. A teenage girl on the birth control pill comes in complaining of shortness of breath and a swollen leg, and a CT scan proves the presence of a massive pulmonary embolus. This is the bread and butter of medical diagnosis—cases where cause and effect tie neatly together and the doctor can almost immediately explain to patient and family whodunit, how, and sometimes even why.

But then there are the other cases: patients with complicated stories or medical histories; cases where the symptoms are less suggestive, the physical exam unrevealing, the tests misleading. Cases in which the narrative of disease strays off the expected path, where the usual suspects all seem to

have alibis, and the diagnosis is elusive. For these, the doctor must don her deerstalker cap and unravel the mystery. It is in these instances where medicine can rise once again to the level of an art and the doctor-detective must pick apart the tangled strands of illness, understand which questions to ask, recognize the subtle physical findings, and identify which tests might lead, finally, to the right diagnosis.

To the doctors caring for Crystal Lessing, it was not clear if the mystery of her illness was going to be solved in time to save her life. Certainly there was no shortage of diagnostic data. There were so many abnormalities it was difficult to distinguish between the primary disease process and those that were the downstream consequences of the disease. The doctors in the ER had focused on her uncontrolled bleeding. Why wasn't her blood clotting? Was this disseminated intravascular coagulopathy (DIC)—a mysterious disorder that frequently accompanies the most severe infections? In this disease the fibrous strands that make up a clot form willy-nilly inside blood vessels. These tough strands slice through red blood cells as they course through the artery, releasing the oxygen-carrying contents and strewing the torn fragments of cells into the circulation. Yet careful examination of Crystal's blood didn't reveal any of these cell membrane fragments. So it wasn't DIC.

And why was she yellow? Hepatitis was the most common cause of jaundice in a young person. But the ER physician found no evidence of any of the several viruses that can cause hepatitis. Besides, the blood tests they'd sent to check how well her liver was working were almost normal. And so, they concluded, it wasn't her liver.

Once Crystal was transferred to the ICU, the doctors there had focused on the bloody diarrhea. She'd had two courses of powerful antibiotics for a dental infection before the diarrhea and fever started. That fit the pattern for an increasingly common infection with a bacterium called *Clostridium difficile*, or *C. diff.*, as it's known around the hospital. The use of antibiotics can set the stage for this bacterial infection of the colon, which causes devastating diarrhea and a severe, sometimes fatal, systemic illness.

The ICU team had looked for the dangerous toxin made by the *C. diff.* bacteria but hadn't found it. Still, that test can miss up to 10 percent of these infections. In fact, it's standard practice to retest for the bacterial toxin three times before believing that the disease isn't present when suspicion for the disease is high. The ICU team started Crystal on antibiotics to treat *C. diff.* anyway—the story of antibiotics followed by bloody diarrhea made that their leading diagnosis.

But Dr. Wagoner, the resident caring for the patient, was unsatisfied with the diagnosis. Too many pieces didn't seem to fit. The antibiotics and diarrhea made sense but the diagnosis left too many of her symptoms unexplained.

That Friday afternoon—forty-eight hours after Crystal was admitted to the hospital—Wagoner did what doctors often do when faced with a complex case: he reached out to a more experienced physician. Despite all the available technology, the tools doctors often rely on most are the most old-fashioned—a phone, a respected colleague, a mentor or friend.

Dr. Tom Manis was one of the most highly regarded doctors in the hospital. A nephrologist, he was called in because of Crystal's kidney failure. But as Wagoner presented the patient to the older doctor, it was clear he was hoping that Manis could help them figure out more than just the kidney.

As Manis read through the chart, he too became alarmed. Wagoner was right—this diagnosis didn't fit well at all. For one thing, *C. diff.* colitis is usually a disease of the sick and elderly. The patient was young and had been healthy. But even more to the point, *C. diff.* wouldn't account for the profound jaundice and the anemia that persisted despite multiple transfusions. So Manis did what the resident had done—"I called every smart doctor I knew," and told them each the perplexing tale of Crystal Lessing—again, using those irreplaceable tools, a phone and a friend. One of those friends was Dr. Steven Walerstein, the head of the hospital's Department of Medicine.

It was early evening by the time Walerstein had a chance to see the patient. He didn't read her chart. He never did in tough cases like this. He didn't want to be influenced by the thinking of those who had already seen

her. Far too often in these difficult cases something has been missed, or misinterpreted. And even if they had collected all the pieces, they had clearly put the story of this illness together incorrectly.

Instead he went directly to the patient's bedside.

Walerstein introduced himself to the young woman and her mother. He pulled up a chair and sat down. Getting the whole story is essential but it can take time. Can you tell me what happened, from the beginning? he asked the sick girl. Like the classic detective in a mystery novel, he asked the victim to go over the crime once more. "I've told this story so many times," Crystal protested. Her voice was thick with fatigue, her words slurred. Couldn't he just read it in her chart? No, he told her gently but firmly. He needed to hear it from her, needed to put it together for himself. Slowly the girl began telling her story once more. Her mother took up the tale when the girl became confused or couldn't remember.

Once the two women had gone through the events that brought each of them to the ICU, Walerstein asked the mother for a little more information about her daughter. Crystal had just graduated from college, she told him. She was working as a nanny while she tried to figure out what she wanted to do with her life. She didn't smoke or drink or use drugs. And she'd never been sick. Never. She roughly brushed away tears as she described her daughter to this kindly middle-aged doctor. He nodded sympathetically. He had a daughter.

Then Walerstein turned back to the young woman in the bed. Her yellow skin was now hot and dry. Her lips were parched and cracked. Her abdomen was distended and soft, but he could feel the firm edge of the liver, normally hidden by the rib cage, protruding a couple of inches below. She moaned again as he put pressure on this tender and enlarged organ.

Only then did he allow himself to look through her chart. He skipped over the notes and buried himself in the myriad abnormal test results that had been collected over her two days in the intensive care unit.

Walerstein was a general internist, admired for his broad knowledge of medicine and his clinical acumen. If he didn't know the answer right off the bat, he was known to ask questions that would lead to the answer. And

this young woman needed an answer, or she would die. Having thoroughly examined the patient and her chart, Walerstein took a moment to step back and look for some kind of pattern buried in the chaos of numbers and tests.

The ICU doctors had focused on the bloody diarrhea and had gotten nowhere. Indeed, although the girl had seen blood in her stools at home, since arriving at the hospital she had very little diarrhea. It didn't seem to Walerstein to be the most important of her symptoms. Instead, Walerstein went back to the striking feature that had caught the ER doctor's eye—her blood would not clot.

The liver makes most of the proteins that cause blood to coagulate. Could it be that her liver was no longer making these proteins? *Could it be that her liver wasn't working at all?* That would account for both the bleeding and the jaundice. But liver failure is usually marked by dramatic elevations in certain enzymes that are released when liver cells are destroyed, and those enzymes had been nearly normal since she'd come to the hospital. Her doctors had taken that to mean that the liver was not involved in this deadly process.

What if, instead, the liver had already been destroyed by the time Crystal came to the hospital? What if these markers of liver injury (known as transaminases) weren't elevated because there were no more liver cells left to injure, if all the liver cells had already been destroyed? No one in the Emergency Department or in the ICU had made this leap. And yet if you looked at it in this way, as Walerstein did, everything made perfect sense. It all fit.

He then turned his attention to the profound anemia that had been noted from the start. Despite multiple transfusions, Crystal still had only half as much blood as she should. She was bleeding—her red-tinted urine showed that—but she wasn't bleeding that much. It was clear that her red blood cells were being destroyed within her body. Deep within her chart there was a test that showed this but Walerstein noted that the team caring for her hadn't considered this in their search for a diagnosis.

Too often information you don't initially understand is simply set aside, especially when there is such a wealth of information. Walerstein under-

stood this phenomenon. And once set aside it's often forgotten. It happens all the time. But Walerstein also knew that in a difficult case like this one, data that has been set aside often holds the key.

So Crystal had liver failure and red blood cell destruction. That combination stirred something deep within his memory. Walerstein could feel the pieces slowly come together like the cogs in some ancient machine. And then suddenly he knew what this was.

The internist hurried to the library to check his hunch. Yes! He was right. This combination—liver failure and red blood cell destruction—was an unusual manifestation of an unusual inherited illness: Wilson's disease.

In Wilson's disease, the liver lacks the machinery to regulate copper, an essential mineral found in the diet. Without these chemical tools, excess copper builds up in the liver and other organs and slowly, insidiously breaks them down. Usually this process takes place over decades, but occasionally, for reasons that are still not understood (though it is often associated with the use of antibiotics, as it was in Crystal's case), the copper blasts out of the liver—destroying the organ in the process—and a lifetime of the stored mineral floods into the bloodstream. Once there, all hell breaks loose: the copper demolishes red blood cells on contact. The kidneys work hard to clear the cell fragments from the circulation but are gravely injured in the process. Meanwhile the high levels of copper in the bloodstream attack virtually every organ in the body. In this form, the disease is rapidly and universally fatal unless the patient receives the only possible cure—a new liver to replace the one destroyed by the jailbreak of copper, a liver that has the machinery to dispose of the excess mineral. If this was Wilson's disease, this patient needed a transplant immediately.

But first Walerstein had to confirm the diagnosis. It was late on a Friday night and so it would be impossible to measure the amount of copper in her blood—in any case, his hospital laboratory didn't even do that test. But there was another way to diagnose this disease. Patients with Wilson's will often accumulate copper in their eyes—a golden brown ring at the very outermost edge of the iris. Walerstein hurried back to the ICU. He carefully examined the girl's eyes. Nothing. He couldn't see the rings, but maybe an

ophthalmologist with his specialized equipment could. “It’s not often that you call the ophthalmologist at nine p.m. on a Friday” to do an emergency examination, Walerstein told me. But he related the girl’s story one more time—this time with a likely diagnosis, if only he could confirm it. “I’m sure he thought I was nuts, until he saw the rings.” As soon as Walerstein had the results, he hurried into the patient’s room to tell the girl and her mother what they’d found.

Crystal Lessing was transferred by helicopter that night to New York–Presbyterian Hospital. Patients with the greatest need get priority in the transplant line. Without a new liver, Crystal would die within days and that put her at the front of the line. She received an organ the following week and survived.

Crystal’s story is every patient’s nightmare: To be sick, even dying, and have doctor after doctor fail to figure out why. To be given the wrong diagnosis, or no diagnosis at all, and to be left to the ravages of disease with nothing more than your own endurance and the doctors’ best-guess therapy to rely on. To live or die in a modern hospital filled with the promise of treatment and yet without a diagnosis to guide its use.

How was Walerstein finally able to make a diagnosis after so many others had failed? How do doctors make these tough diagnoses? Walerstein is modest about his role in the case. “I think I was just lucky enough to know about this rare form of this rare disease. No one can know everything in medicine. I happened to have known about this,” he told me. It’s sometimes a mysterious process—even to the doctors themselves. “A bell went off and the connection was made,” Walerstein told me. “That’s all I know.”

This book is about that bell—how doctors know what they know and how they apply what they know to the flesh-and-blood patient who lies before them. It can be a messy process, filled with red herrings, false leads, and dead ends. An important clue may be overlooked in the patient’s history or examination. An unfamiliar lab finding may obscure rather than reveal. Or

the doctor may be too busy or too tired to think through the case. Even the great William Osler must have had his bad days.

And the patient, by definition sick, frequently tired and in pain, inarticulate with distress, is given the essential task of telling the story that could help a doctor save his life. It's a recipe for error and uncertainty. It is "an inferential process, carried out under conditions of uncertainty, often with incomplete and sometimes inconsistent information," says Jerome Kassirer, former editor of the *New England Journal of Medicine* and one of the earliest and most thoughtful modern writers on this unruly process.

It's a wayward path to an answer filled with unreliable narrators—both human and technological—and yet, despite the unlikeliness, that answer is often reached and lives are saved.

Often, but not always. The possibility of error is ever present.

It's certainly not news that medical errors are common. In 1999 the National Institutes of Health (NIH), Institute of Medicine, released a report on the topic—*To Err Is Human*. In that now famous report the authors concluded that there were up to 98,000 patient deaths due to medical errors every year—the same number of deaths we would see if a jumbo jet crashed every day for a year. That set off a national effort to reduce the rate of errors in medicine that is still bearing fruit.

That report did not look at errors in diagnosis. And yet errors in diagnosis make up a large chunk of the errors made in medicine. Depending on which study you believe, it is the first or second most common cause of medical lawsuits. Studies suggest that between 10 and 15 percent of patients seen in primary care specialties—internal medicine, family medicine, and pediatrics—are given an incorrect diagnosis. Often the error has no effect—people get better on their own or return to their doctor when the symptoms get worse—but doctors and patients alike worry about the possibility of a diagnostic error that hurts or even kills. In a study of over thirty thousand patient records, researchers found that diagnostic errors accounted for 17 percent of adverse events.

Doctors are getting better at making diagnoses. Tests and imaging have made possible diagnoses that were in earlier times only knowable at autopsy. And while postmortem studies done in this country suggest that the rate

of unsuspected diagnoses has been remarkably stable over the past several decades, that statistic is skewed by the diminishing number of autopsies performed. A study done at the University Hospital in Zurich, Switzerland, where there is a 90 percent autopsy rate, shows that over the past few decades the number of missed or erroneous diagnoses has steadily dropped. Another study done for the Agency for Healthcare Research and Quality (the AHRQ, a research arm of the NIH) shows a similar trend in this country if you account for the ever shrinking pool of autopsies.

Still, the fear of getting it wrong is always present for both doctors and patients. As a result, there is a new and growing interest in better understanding diagnostic errors in medicine. The first-ever conference on the topic—one of the earliest signs of growing research interest—was held in Phoenix in 2008. And the AHRQ, the government agency charged with improving the quality of health care in this country, offered its first grants for research on the topic in the fall of 2007.

Research into diagnostic error, like research into the diagnosis process itself, is still a very new field. There is even difficulty in deciding what constitutes a diagnostic error. What a thoughtful patient may consider an error is not necessarily the same as that which his equally thoughtful doctor might consider an error.

For example, when a patient comes to my office with a sore throat and a fever, I might check for strep, and if it's not present I'll probably send him out with a diagnosis of a viral illness. But I share with all such patients what I expect to happen over the next few days—that they should start to feel better within a day or two. And if not, I tell them to call me and let me know. Because, while the odds are overwhelming that this is simply a viral syndrome, it's not 100 percent certain. I might be wrong. The test might be wrong. It might be mono. It might be some other kind of bacterial tonsillitis. It might be cancer.

I can't just check under the hood and see if the spark plugs need to be replaced—the way a mechanic diagnoses the funny noise your car is making. Instead, I have to listen to the engine and, based on the indirect evidence I can collect, make a thoughtful and well-informed guess as to what is *probably* going on.

If I send that patient home with a diagnosis of a viral syndrome and he doesn't get better and has to come back, would that be a diagnostic error? I suspect the patient would think so. And certainly it wasn't a correct diagnosis. But did I make an error? Should I have done something different?

I could have been more certain. I could have sent my patient to an Ear, Nose, and Throat specialist who could have looked down his throat with a special scope. I could have even asked for a biopsy of the red and swollen tissue to confirm my diagnosis. That would be time-consuming and painful for the patient and ridiculously expensive. But even then, the diagnosis would not have been 100 percent certain. In medicine, uncertainty is the water we swim in.

The chance of being wrong is overwhelming when dealing with something more complicated than a sore throat. Doctors—far more than the patients they care for—recognize that some error is inevitable. From the first moment a doctor sets eyes on a patient, she begins to formulate a list of possible causes of the symptoms—what's known as a differential diagnosis. As the story emerges, that list is modified—diseases on the list disappear to be replaced by new ones that more closely adhere to the patient's story, or exam, or sometimes test results. By the end of the encounter the doctor has a list of likely suspects.

If the doctor has worked through the problem well, there's a very good chance that one of these possible diagnoses will be right. The rest though, by definition, will be wrong. We are regularly wrong in the pursuit of being right. It's important to have a list of possibilities because medicine is complicated and diseases and bodies differ. We frequently have a diagnosis that we consider most likely, but we're taught also to come up with a plan B because our patients don't always have the most likely disease. The question we are taught to ask ourselves is, if it isn't that, what else could it be?

As a collector of diagnostic stories, I find myself frequently asking why one doctor was able to make the diagnosis when others before her couldn't. Where were the errors? How were they made? What can we learn?

Sometimes the problem is a lack of knowledge. This was certainly the case in Crystal Lessing's story. She had a rare presentation of an unusual disease. One of the human limitations in medicine is that no one can know everything.

There were errors in thinking in Crystal's case as well. Recognizing that the fundamental problem was liver failure was an essential step in Walerstein's thinking process—a realization that eluded all of the doctors who had seen her initially.

There were also mistakes in some of the data collected from the patient. Walerstein noted that the patient's "bloody diarrhea" consisted of a couple of episodes of bloody stools the day she came to the hospital. And Walerstein was also the first to note the enlarged and tender liver when he examined the young woman—a hint that the organ wasn't as normal as the blood tests suggested. Abnormalities uncovered by testing were also not interpreted correctly. Crystal's jaundice was initially attributed to the destruction of the red blood cells. Yet when further testing revealed that this red-blood-cell massacre was not the result of an abnormal immune system improperly attacking the cells, Walerstein was the first to consider other causes of red cell destruction. Research suggests that diagnostic errors—like this one nearly was—are often due to a multitude of missteps made along the way.

The solution to this case, as with so many cases, lay in the proper use of all the tools we have at our disposal. Walerstein took a careful history, performed a thorough physical examination, and identified the important lab abnormalities. Only then was he able to connect the information about that patient with the knowledge he had to make the diagnosis. Only then did the pieces of the puzzle come together.

In telling you these stories I try to put you, the reader, in the front line, in the shoes of the doctor at the bedside—to know that feeling of uncertainty and intrigue when confronted with a patient who has a problem that just might kill him. I try to show you the mind of the physician at work as she struggles to figure out exactly what is making the patient sick. To do this I

have divided this book according to the steps we take in the evaluation of each and every patient we see. Each chapter focuses on one of the tools of our trade, how it's supposed to work, and how errors send us astray. As physicians become more open about what we do, we make it easier for patients to understand what they can do to more fully participate in their own care.

This book has its roots in a column I have written for the past six years for the *New York Times Magazine*. The column has been my opportunity to share with general readers my personal collection of fascinating diagnostic histories. It's a collection I began (unwittingly) to assemble years ago, while my own medical career was still in its formative stages.

I came to medical school as a second career. The first I spent in television news, mostly covering medicine, mostly for CBS. I hadn't planned to go to medical school; it wasn't some long deferred dream. But one day, while filming with television correspondent Dr. Bob Arnot, I watched him save an elderly woman's life. He was supposed to be shooting a stand-up on white-water rafting when he suddenly disappeared from the raft I was watching in the monitor. The cameraman and I searched the distance and saw him on the banks of the river, pulling an elderly woman onto the rocky shore. The cameraman refocused on this new image and I watched with fascination as Bob performed basic cardiopulmonary resuscitation (CPR) and brought the nearly drowned woman back to life.

I didn't quit television right then and there and head off to medical school, but it planted an idea and revealed a hidden dissatisfaction with my role in TV. Television reaches millions, but touches few. Medicine reaches fewer but has the potential to transform the lives of those it touches.

So I did two years of premed at Columbia University, then applied and was accepted at the Yale School of Medicine. I completed my residency training at Yale's Primary Care Internal Medicine program and have stayed on here to care for patients and teach new generations of doctors.

When I started medical school I thought I would be most interested in pathophysiology—the science behind what goes wrong when we get sick.

And, in fact, I loved that subject and still do. But what captured my imagination were the stories doctors told about their remarkable diagnoses—mysterious symptoms that were puzzled out and solved. These were the stories I found myself telling my husband and friends at the dinner table.

Covering medicine for as many years as I had, I thought I understood how medicine worked. But these stories revealed a new aspect of medicine—one well known to doctors but rarely discussed outside those circles. In writing my columns and now this book, I try to share a face of medicine that is both exciting and important. Exciting because the process of unraveling the mystery of a patient's illness is a wonderful piece of detective work—complicated yet satisfying. Important because any one of us might someday be that patient. The more you know about the process, the better you will be prepared to assist and understand.

PART ONE



Every Patient Tells a Story

CHAPTER ONE

The Facts, and What Lies Beyond

The young woman was hunched over a large pink basin when Dr. Amy Hsia, a resident in her first year of training, entered the patient's cubicle in the Emergency Department. The girl looked up at the doctor. Tears streamed down her face. "I don't know if I can take this any longer," twenty-two-year-old Maria Rogers sobbed. Since arriving at the emergency room early that morning, she'd already been given two medicines to stop the vomiting that had brought her there—medicines that clearly had not worked.

"I feel like I've spent most of the last nine months in a hospital or a doctor's office," Maria told the doctor quietly. And now, here she was again, back in the hospital. She'd been perfectly healthy until just after last Christmas. She'd come home from college to see her family and hang out with her friends, and as she prepared to head back to school this strange queasiness had come over her. She couldn't eat. Any odor—especially food—made her feel as if she might vomit. But she didn't. Not at first.

The next day, on the drive back up to school, she'd suddenly broken into a cold sweat and had to pull over to vomit. And once she got started, it seemed like she would never stop. "I don't know how I made it to school because it seems like I had to get out of the car to throw up every few minutes."

Back at school she spent the first few days of the semester in bed. Once she was back in class her friends joked that she was just trying to get rid of

the extra pounds from the holidays. But she felt fine and she wasn't going to worry about it.

Until it happened again. And again. And again.

The attacks were always the same. She'd get that queasy feeling for a few hours, and then the vomiting would start and wouldn't let up for days. There was never any fever or diarrhea; no cramps or even any real pain. She tried everything she could find in the drugstore: Tums, Pepcid, Pepto-Bismol, Prilosec, Maalox. Nothing helped. Knowing that another attack could start at any moment, without warning, gnawed insistently in the back of her mind.

She went to the infirmary with each attack. The doctor there would get a pregnancy test and when it was negative, as it always was, he'd give her some intravenous fluids, a few doses of Compazine (a medicine to control nausea), and, after a day or two, send her back to the dorm. Halfway through the semester she withdrew from school and came home.

Maria went to see her regular doctor. He was stumped. So he sent her to a gastroenterologist, who ordered an upper endoscopy, a colonoscopy, a barium swallow, a CT scan of her abdomen, and another of her brain. She'd had her blood tested for liver disease, kidney disease, and a handful of strange inherited diseases she'd never heard of. Nothing was abnormal.

Another specialist thought these might be abdominal migraines. Migraine headaches are caused by abnormal blood flow to the brain. Less commonly, the same kind of abnormal blood flow to the gut can cause nausea and vomiting—a gastrointestinal equivalent of a migraine headache. That doctor gave Maria a medicine to prevent these abdominal "headaches" and another one to take if an attack came anyway. When those didn't help, he tried another regimen. When that one failed, she didn't go back.

The weird thing was, she told Hsia, the only time she felt even close to normal during these attacks was when she was standing in a hot shower. Couldn't be a cold shower; even a warm shower didn't quite do it. But if she could stand under a stream of water that was as hot as she could tolerate, the vomiting would stop and the nausea would slowly recede. A couple of times she had come to the hospital only because she'd run out of hot water at home.

Recently, a friend suggested that maybe this was a food allergy, so she gave up just about everything but ginger ale and saltines. And that seemed to work—for a while. But two days ago she'd woken up with that same bilious feeling. She'd been vomiting nonstop since yesterday.

Maria Rogers was a small woman, a little overweight with a mass of long brown hair now pinned back in a barrette. Her olive skin was clear though pale. Her eyes were puffy from crying and fatigue. She looked sick, and was clearly distressed, Hsia thought, but not chronically ill.

How often did she get these bouts of nausea? she asked the girl. Maybe once a month, she told her. Are they linked to your periods? Hsia offered hopefully. The girl grimaced and shook her head. Are they more common just after you eat? Or when you're hungry? Or tired? Or stressed? No, no, no, and no. She had no other medical problems, took no medicines. She was a social smoker—a pack of cigarettes might last a week, sometimes more. She drank—mostly beer, mostly on the weekends when she went out with her friends.

Her mother had been an alcoholic and died several years earlier. After leaving college she had been living with her father and sister but a few months ago moved into a nearby apartment with some friends. She had no pets, had not traveled within the past year. Had never been exposed to any toxins as far as she knew. Hsia examined her quickly. The gurgling noises of the abdominal exam were quieter than normal and her belly was mildly tender, but both findings could simply be due to the vomiting. There was no sign of an inflamed gallbladder. No evidence of an enlarged liver or spleen. The rest of the exam was completely unremarkable. “As I walked out that door,” Hsia explained to me, “I knew I was missing something but I had no idea what it was. Or even what to look for.”

More Than Just the Facts

Dr. Hsia was a resident in Yale's Primary Care Internal Medicine residency training program, where I now teach. She told me about Maria Rogers because she knew I collected interesting cases and sometimes wrote about

them in my column in the *New York Times Magazine*. In thinking about this case, Amy told me she knew from the start that if she was going to figure out what was causing this patient to suffer so, it wasn't going to be because she had greater knowledge—because Maria Rogers had already seen lots of experts. No, if she was going to figure it out, it would be because she'd find a clue that others had overlooked.

The patient's story is often the best place to find that clue. It is our oldest diagnostic tool. And, as it turns out, it is one of the most reliable as well. Indeed, the great majority of medical diagnoses—anywhere from 70 to 90 percent—are made on the basis of the patient's story alone.

Although this is well established, far too often neither the doctor nor the patient seems to appreciate the importance of what the patient has to say in the making of a diagnosis. And yet this is crucial information. None of our high-tech tests has such a high batting average. Neither does the physical exam. Nor is there any other way to obtain this information. Talking to the patient more often than not provides the essential clues to making a diagnosis. Moreover, what we learn from this simple interview frequently plays an important role in the patient's health even after the diagnosis is made.

When you go to see a doctor, any doctor, there is a very good chance that she will ask you what brought you in that day. And most patients are prepared to answer that—they have a story to tell, one that they have already told to friends and family. But the odds are overwhelming that the patient won't have much of an opportunity to tell that story.

Doctors often see this first step in the diagnostic process as an interrogation—with Dr. Joe Friday getting “Just the facts, ma'am,” and the patient, a passive bystander to the ongoing crime, providing a faltering and somewhat limited eyewitness account of what happened. From this perspective, the patient's story is important only as a vehicle for the facts of the case.

Because of that “facts only” attitude, doctors frequently interrupt patients before they get to tell their full story. In recordings of doctor-patient encounters, where both doctor and patient knew they were being taped, the doctor interrupted the patient in his initial description of his symptoms over 75 percent of the time. And it didn't take too long either. In one study

doctors listened for an average of sixteen seconds before breaking in—some interrupting the patient after only three seconds.

And once the story was interrupted, patients were unlikely to resume it. In these recorded encounters fewer than 2 percent of the patients completed their story once the doctor broke in.

As a result, doctors and patients often have a very different understanding of the visit and the illness. Survey after survey has shown that when queried after an office visit, the doctor and patient often did not even agree on the purpose of the visit or the patient's problem. In one study, over half of the patients interviewed after seeing their doctor had symptoms that they were concerned about but did not have a chance to describe. In other studies doctor and patient disagreed about the chief complaint—the reason the patient came to see the doctor—between 25 to 50 percent of the time. This is information that can come only from the patient and yet, time after time, doctors fail to obtain it. Dr. George Balint, one of the earliest writers on this topic, cautioned: "If you ask questions you will get answers, and nothing else." What you won't get is the patient's story, and that story will often provide not only the whats, wheres, and whens extracted by an interrogation, but often the whys and hows as well.

Moreover, the interrogation model makes assumptions about the elicited symptoms and diseases. And while these assumptions might be true for most of the people with those symptoms, they may not be true for this particular individual. The great fictional detective Sherlock Holmes talks at length about the difference between the actions and thoughts of the individual when contrasted to the average. Holmes tells Watson that while you may be able to say with precision what the average man will do, "you can never foretell what any one man will do." The differences between the average and the individual may not be revealed if the doctor doesn't ask.

"It is much more important to know what kind of patient has the disease than what sort of disease the person has," Osler instructed his trainees at the turn of the twentieth century. Even with all of our diagnostic technology and our far better understanding of the pathophysiology of disease, research suggests this remains true.

So getting a good history is a collaborative process. One doctor who writes frequently about these issues uses the metaphor of two writers collaborating on a manuscript, passing drafts of the story back and forth until both are satisfied. “What the patient brings to the process is unique: the particular and private facts of his life and illness.” And what the physician brings is the knowledge and understanding that will help him order that story so that it makes sense both to the doctor—who uses it to make a diagnosis—and to the patient—who must then incorporate that subplot into the larger story of his life.

If getting a good history is so important to making an accurate diagnosis, why are we so bad at it? There are several reasons.

First, most researchers, doctors, and patients would agree that time pressures play an important role. A visit to a doctor’s office lasts an average of twenty-two minutes. Although there is a sense that doctors are spending less time with their patients, that number has actually increased over the past twenty years. In 1989, the average doctor’s appointment lasted only sixteen minutes. Despite this extra time, both doctors and patients frequently agree that their time together is still too short.

In response, doctors often depend on a few highly focused questions to extract the information they think will help them make a diagnosis quickly. Yet it is clear that this effort to reduce the time it takes to get a good history increases the risk of miscommunication and missed information. Like so many shortcuts, this information shortcut often ends up taking more time than those interviews in which patients are able to tell their stories in their own ways.

Studies suggest that getting a good history allows doctors to order fewer tests and make fewer referrals—without taking any more time. Indeed, some studies suggest that obtaining a good history can even reduce visit time. In addition, patient satisfaction is higher, adherence to therapy is higher, symptom resolution is faster, lawsuits are less frequent.

Lack of training may also contribute to the problem. Doctors spend two years in classrooms learning how to identify and categorize disease processes, matching symptoms to known disease entities, but until recently very few

programs offered any training on how to obtain that essential information. The assumption seemed to be that this did not need to be taught. And there may have been an unspoken expectation that our improved diagnostic technology would reduce our dependence on this kind of personal information. Studies have shown that neither assumption is true, and now most medical schools offer classes in doctor-patient communication. Moreover, since 2004, medical students are required to demonstrate proficiency in their history-taking skills in order to become licensed physicians. A new generation of physicians may not use these tools, but at least they have them.

Finally, many doctors are uncomfortable with the emotions that are sometimes associated with illness. When patients present their stories, they often look for cues from the doctor as to what type of information they should give. The interrogation format tells the patient that what's needed from them are the facts and only the facts. And yet illness is often much more than a series of symptoms. The experience of being sick is frequently interlaced with feelings and meanings that shape and color a patient's experience and perception of a disease in ways that are unimaginable, and unanticipated, by the doctor. A family history of heart disease or cancer may lead a patient to minimize a symptom. I recently got a phone call from a friend, a man in his late fifties whose father had heart disease. My friend was having chest pains when he walked up a hill. He wondered if this was his childhood asthma returning. He was shocked when I suggested he see a cardiologist. He had two blocked arteries, which were opened with complete resolution of his pain. The same history might cause another to focus on a symptom well beyond its actual severity. I have a few patients who have had many stress tests because of their concerns over their chest pain. The fact that previous tests have not shown heart disease provides them with no comfort or reassurance. Financial concerns may likewise affect how patients tell their stories.

Worries about the social meaning of symptoms can complicate even a straightforward diagnosis. I learned this the hard way. A patient I saw when I was a resident came for a school physical. She was young and healthy. As I was finishing up and preparing to move on to the next patient, she sud-

denly asked me about a lesion on her buttocks. Could it be from doing sit-ups on the hard floor? she asked somewhat anxiously. I quickly looked at the lesion. It looked like a small blister, located in the cleft between the buttocks. Certainly, I reassured her, glancing at my watch. I noticed that she seemed worried about the lesion, but I didn't ask any further questions or do a more thorough exam because I was running behind schedule. Only when the lesion reappeared months later did she acknowledge that her boyfriend had had a breakout of genital herpes on a vacation they'd taken together and she hadn't insisted on his use of a condom. The reappearance of the lesions made herpes the likely culprit. I completely missed a straightforward diagnosis because I was too rushed to address her anxiety and she was too embarrassed to offer this other history. It happens all the time.

Everybody Lies

Several years ago I got a call from a producer named Paul Attanasio. He had created a television show based in part on my column in the *New York Times Magazine* and wanted to know if I would be interested in being a consultant for this new show. It was a drama, he told me, about an ornery doctor who was a brilliant diagnostician. I agreed to work on the show, thinking that it wasn't going to last long. The show, called *House M.D.*, quickly found an enthusiastic audience.

In this show, Dr. Gregory House doesn't value patient history. Indeed, he frequently tells his trainees that they should not believe a patient's version of his illness and symptoms, because "Everybody lies." In the context of the show, there is a certain truth in that. Patients frequently lie to House and sometimes his staff—not because the patients are intrinsically deceitful but because of who House is. As portrayed (brilliantly by Hugh Laurie), House is far from the kindly and gentle doctor whose presence invites trust and confidences. Instead, he is narcissistic and arrogant, a drug addict, and something of a pedant. He is a darker, more bitter version of Conan Doyle's brooding detective Sherlock Holmes. House's demeanor tells patients that

the feelings and meanings illness may have for them are not important and so they don't tell him about them. As a result, House often gets only part of their story.

The mystery is solved only when the rest of their story is revealed—either from evidence found when his staff break into the patient's home (a quirky twist on getting a thorough history) or when the patient is finally forced to reveal his hidden truths. House acknowledges the importance of a thorough patient history but concludes that the problem is the patient who lies rather than the doctor who fails to establish a relationship in which difficult, embarrassing, or distressing truths can be told.

Amy Hsia knew from the start that if she was going to figure out the cause of Maria Rogers's cyclic episodes of vomiting, it would be because of some key piece of history that she was able to get that others had overlooked. But sitting outside the patient's room that afternoon, she wasn't sure she'd found it. She went through the thick charts, reading the notes and test results collected by all of the other doctors involved in the same exercise in previous hospitalizations, trying to make it all make sense. Nothing leaped out at her. The sketchy description of the symptoms and history provided nothing she hadn't already found out from the patient herself.

Hsia considered the differential diagnosis once more. Nausea and vomiting have a very long list of causes: ulcers, gallstones, obstruction, infection. Hepatitis, pancreatitis, colitis, strokes, and heart attacks. None of them seemed to fit in a case of a young woman with multiple episodes of vomiting and lots and lots of tests showing no abnormalities. Maybe she wasn't going to be able to figure this patient out either. She ordered a new medication to relieve the nausea and then moved on to see her next patient.

The next morning, when Dr. Hsia, her supervising resident, and the attending physician—the troika of the modern hospital medical patient care team—visited Ms. Rogers, the girl's bed was empty. The sound of the shower told them where she'd gone. That caught the young resident's attention. When she had come by a couple of hours earlier to examine the girl, she'd

been in the shower then too. She remembered that Rogers had told her that her nausea improved when she took a shower. What kind of nausea didn't get better with the traditional nausea medications—by now she'd been on most of them—but improved with a hot shower?

Hsia posed the question to the team. Neither had heard of such a syndrome. So, after the team had finished seeing all the patients they were caring for, Hsia hurried to find a computer. She went to Google and entered "persistent nausea improved by hot showers." She hit the enter key and less than a second later the screen was filled with references to a disease Hsia had never heard of: cannabinoid hyperemesis—persistent and excessive vomiting (hyperemesis) associated with chronic marijuana use (cannabinoid).

The disorder was first described in 1996, in a case report from an Australian medical journal. Dr. J. H. Allen, a psychiatrist in Australia, described a patient admitted to his care with a diagnosis of psychogenic vomiting—vomiting due to psychological rather than physiological causes. Allen noticed that this patient's vomiting was associated with a bizarre behavior—repetitive showering. He took a dozen showers each day. Allen also noticed that the symptoms improved over the course of his hospitalization but recurred when the patient was sent home. The patient had a long history of chronic heavy marijuana use and Allen hypothesized that the vomiting might be triggered by the marijuana.

Over the next several years Allen noted similar patterns in other patients admitted with vomiting disorders, and in 2001 he published a paper reporting on ten patients with the disorder he named cannabinoid hyperemesis. Each patient in his series smoked marijuana daily; each had developed intermittent nausea and vomiting. All had used marijuana for years before they developed these episodic bouts of nausea and vomiting. And remarkably, nine of the ten patients reported that hot showers helped their symptoms when everything else failed. All symptoms resolved when these patients gave up marijuana. And then reappeared in three of the ten who resumed their cannabis use. Other case reports followed from around the world.

Could this be what was plaguing Hsia's patient? Did Maria Rogers even smoke marijuana? Hsia hurried back to the patient's room. She found the

patient sitting in bed, a towel wrapped around her still wet hair. Yes, she did smoke marijuana frequently. Maybe not every day but most days. That clinched it—at least in Hsia's mind. The young doctor felt like cheering. She'd figured it out when even the experts had been stumped! This is really one of the great pleasures in medicine—to put the patient's story together in a way that reveals the diagnosis.

She excitedly explained to the patient what she'd found on the Internet—that there was a good chance that marijuana was causing her nausea. She got better in the hospital because she didn't use it when she was here. But when she got home and resumed her regular exposure to the drug, the nausea would once again be triggered. All she had to do was to give up smoking marijuana, Hsia concluded triumphantly, and her symptoms would be cured forever.

This story, which seemed so logical and reasonable from Hsia's perspective, did not make the same kind of sense to the woman who was living it every day. Rogers's response was immediate and emphatic and—to Hsia—shocking. “That is total bullshit. I don't buy it,” the patient snapped angrily. She knew many people who used marijuana a lot more than she did and they didn't get sick like this. How could Hsia explain that? Huh? Besides, wasn't marijuana supposed to help people who were sick from chemotherapy? Why would it decrease nausea in that case and cause nausea in her? she demanded. Where was her proof? Where was her evidence?

Hsia was taken aback by the patient's anger. She thought the young woman would be thrilled by the news that simply stopping the marijuana use would cure her of this devastating illness. Why was she so angry?

Later that morning, Hsia told the attending and resident what she'd found and how angry the patient had become when she told her about this diagnosis. It made sense to the other doctors caring for the patient. The marijuana use, the cyclic nature of the symptoms, and the restorative powers of the hot shower made it seem like a slam dunk. But how were they going to convince the patient?

They never got the chance. Maria Rogers left the hospital the following day. When contacted several weeks later, Rogers reported that the nausea

had recurred. Yes, she had resumed her usual practice of smoking marijuana most days because she still didn't believe there was a link. She had arranged for an evaluation by a gastroenterologist at Yale. When I spoke with Ms. Rogers afterward, she told me that the doctors there had ordered many of the same tests her previous doctors had gotten. Not surprisingly, the results were no different. From Maria's perspective, what she had was still a mystery.

In medicine, the patient tells the story of his illness to the doctor, who reshapes the elements of that story into a medical form, into the language of medicine. The doctor will usually add to the story, incorporating bits of information gleaned through questions, from the examination of the body, from the tests that have been performed—and the result should be a story that makes sense—where all pieces ultimately add up to a single, unifying diagnosis.

But the story of the illness can't stop there. Once the diagnosis is made, the doctor has to once again reshape the story she has created—the story that helped her make the diagnosis—into a story she can then give back to the patient. She has to translate the story back into the language and the context of the patient's life so that he can understand what has happened to him and then incorporate it into the larger story of his life. Only when a patient understands the disease, its causes, its treatment, its meaning, can he be expected to do what is needed to get well.

Studies have repeatedly shown that the greater the patient's understanding of his illness and treatment, the more likely it is that he will be able to carry out his part in the treatment. Much of this research has been done in patients who have been diagnosed with diabetes. Patients who understand their illness are far more likely to follow a doctor's advice about how to change their diet and how to take their medications than those who do not.

It's understandable. Taking medications on a regular basis isn't easy. It requires dedication on the part of the patient. Motivation. A desire to in-

corporate this inconvenient addition into a life that is already complicated. Greater understanding by the patient has been shown to dramatically improve adherence. This is where getting a good history—one that provides you with some insight into the patient and his feelings about his illness, his life, his treatment—can really pay off.

To go back to the story of Maria Rogers, Hsia told me how surprised she was when the patient didn't accept her explanation of her illness. That marijuana was linked to the nausea and vomiting seemed obvious to Dr. Hsia. It was not obvious to Ms. Rogers. Perhaps there was no way for Hsia to explain this to her that would have been acceptable. The story Hsia told to this patient was the doctor's story—the observations and research that allowed Hsia to make the diagnosis. What she didn't do was create the patient's version of the story—one that would make sense in the larger context of her life.

And then the patient left the hospital and with her their chance to figure out how to help her understand her illness. Dr. Hsia tried to stay in touch with Maria after she left the hospital, but after several months the cell phone number she gave was disconnected and a letter was returned. And so, having rejected one diagnosis and the treatment option it suggested, Maria Rogers still suffers from a malady for which she has no name and no cure.

Stories That Heal

One of the most important and powerful tools a doctor has lies in her ability to give a patient's story back to the patient, in a form that will allow him to understand what his illness is and what it means. Done successfully, this gift helps the patient incorporate that knowledge into the larger story of his life. Through understanding, the patient can regain some control over his affliction. If he cannot control the disease, he can at least have some control over this response to the disease. A story that can help a patient make sense of even a devastating illness is a story that can heal.

The primary work of a doctor is to treat pain and relieve suffering. We

often speak of these two entities as if they were the same thing. Eric Cassell, a physician who writes frequently about the moral dimensions of medicine, argues, in a now classic paper, that pain and suffering are very different. Pain, according to Cassell, is an affliction of the body. Suffering is an affliction of the self. Suffering, writes Cassell, is a specific state of distress that occurs when the intactness or integrity of the person is threatened or disrupted. Thus, there are events in a life that can cause tremendous pain, and yet cause no suffering. Childbirth is perhaps the most obvious. Women often experience pain in labor but are rarely said to be suffering.

And those who are suffering may have no pain at all. A diagnosis of terminal cancer, even in the absence of pain, may cause terrible suffering. The fears of death and uncontrollable loss of autonomy and self combined with the fear of a pain that is overwhelming can cause suffering well before the symptoms begin. There are no drugs to treat suffering. But, says Cassell, giving meaning to an illness through the creation of a story is one way in which physicians can relieve suffering.

In the case of Maria Rogers, Dr. Hsia was able to gather the data necessary to make a diagnosis. She knew the disease the patient had. And yet she didn't know enough about the person who had the disease. The story she gave back to the patient was a reasonable one and a rational one, but it was not one the patient could accept. And when confronted with the vehement rejection of that story and the raw emotion displayed, Hsia retreated. Before she was able to regroup and try again, the patient left her care. Rogers rejected Hsia's story, rejected her diagnosis, and, when last I spoke with her, continued to search on her own for an end to her pain and suffering.

And yet the right story has nearly miraculous powers of healing. A couple of years ago I got an e-mail from a patient whose remarkable recovery highlighted the difference between pain and suffering and the healing power of the story. Randy Whittier is a twenty-seven-year-old computer programmer who was in perfect health and planning to get married when suddenly he began to forget everything. It started one weekend when he and his fiancée traveled to her hometown to begin making the final arrangements for their wedding the following spring. He had difficulty concentrating and was fre-

quently confused about where they were going and whom they were talking with. He chalked it up to fatigue—he hadn't been sleeping well for some time—and didn't say anything to his fiancée. But on Monday morning, when he went back to work, he realized he was in trouble and sent an instant message to his fiancée, Leslie.

Leslie saw the flashing icon on her computer announcing that an instant message had arrived. She clicked on it eagerly.

"Something's wrong," the message read.

"What do you mean?" she shot back.

"My memory is all f'ed up. I can't remember anything," he wrote. Then added: "Like I can't tell you what we did this weekend."

Leslie's heart began to race. Her fiancé had seemed distracted lately. She thought maybe he was just tired. But he'd been strangely quiet on their trip to New York this weekend. He had been excited when they set up the trip, and she'd worried that he was getting cold feet.

"When is our wedding date?" she quizzed him. If he could remember anything, he'd be able to remember that. Planning this wedding had dominated their life for the past several months. "Can you tell me that?"

"No."

"Call the doctor. Do it now. Tell them this is an emergency."

Over the next half hour, Randy put in three calls to his doctor's office, but each time he had forgotten what they told him by the time he messaged his fiancée. Separated by miles of interstate and several suburbs, Leslie was frantic. Finally, at her insistence, Randy, now terrified, asked a friend to take him to the closest hospital.

A few hours later, her cell phone rang. At last. He was being discharged, he told her. The emergency room doctor thought his memory problems were caused by Ambien, the sleeping pill he was taking. The doctor said the symptoms would probably improve if he stopped taking the medication.

Leslie didn't buy that for a second. "Don't go anywhere," she instructed him. "I'll pick you up. I'm going to take you to your doctor." A half hour later she found Randy wandering down the street in front of the hospital, uncertain about why he was there and even what her name was. She hustled

him into the car and drove to his doctor's office. From there they were sent to Brigham and Women's Hospital in Boston.

Late that night, the on-call resident phoned Dr. William Abend at home to discuss the newest admission. Abend, a sixty-one-year-old neurologist, scrolled through the patient's electronic medical record as the resident described the case. The patient, who had no history of any previous illnesses, had come in complaining of insomnia and severe memory loss. Psych had seen him—he wasn't crazy. His physical exam was normal except he didn't know the date and he couldn't recall the events of the week or even that day. The ER had ordered an MRI of his brain but it hadn't been done yet.

The patient needed a spinal tap, Abend instructed, to make sure this wasn't an infection, and an EEG, an electroencephalogram, to see if he was having seizures. Both could affect memory. He'd see the patient first thing the next morning.

Randy was alert and anxious when Abend came to see him. Tall and slender with earnest blue eyes, the young patient seemed embarrassed by all that he couldn't remember. His fiancée had gone to get some rest, and so his mother provided the missing details. He'd first complained about some memory problems a couple of months earlier. The past weekend everything got much, much worse. He couldn't remember anything from the past few days. He couldn't even remember he was in the hospital. Overnight, he repeatedly pulled out his IV.

On exam, Abend found nothing out of the ordinary save the remarkable degree of short-term memory loss. When Abend asked the patient to remember three words—automobile, tank, and jealous—the patient could repeat them but thirty seconds later he could not recall even one. "It wasn't like—where did I put my car keys?" Abend told me. "He really couldn't remember anything." The neurologist knew he had to determine what was going on quickly, before further damage was done.

Abend checked the results of the spinal tap—there were no signs of infection. Then he headed over to radiology to review the MRI. There was no evidence of a tumor, stroke, or bleeding. What the MRI revealed were areas

that appeared bright white in the normally uniform gray of the temporal lobe on both sides of the brain.

There are only a few diseases that would cause this kind of injury. Viral encephalitis—an infection of the brain that is often caused by herpes simplex—was certainly the most common. Autoimmune diseases like lupus could also cause these kinds of abnormalities. In lupus, the body's natural defenses mistakenly attack its own cells as if they were foreign invaders. Finally, certain cancers can do this too—it's usually lung cancer, usually in older smokers.

The young man's symptoms had been coming on gradually over two months. Abend thought that made an infection like herpes less likely. The patient had already been started on acyclovir—the drug usually used to treat herpes encephalitis—since the disease can be deadly when it infects the brain. Although Abend thought it unlikely, they would need to do additional tests of the spinal fluid to make sure there was no evidence of this dangerous viral infection.

Lupus seemed even more unlikely to Abend. It is a chronic disease that can attack virtually any organ in the body and is generally characterized by joint pains and rashes. The patient had none of these symptoms. Still, perhaps this was the first sign of this complex disease. It would be unusual, but so was the young man's extensive memory loss.

Although cancer was an uncommon cause of this kind of injury, it seemed to Abend the most credible in this patient. Even nonsmokers can get lung cancer. And other cancers can cause the same type of brain injury. Moreover, if these symptoms were caused by a cancer, there was a good chance that they would resolve once the cancer was treated. He ordered a CT of the chest, abdomen, and pelvis. Ordering all of these scans communicates uncertainty about what you are looking for and where it might be located, but Abend felt strongly that they didn't have time to be wrong.

Results from the tests trickled in over the next few days. He wasn't having seizures. It wasn't a virus. He didn't have lupus. But by the time those test results arrived they already had an answer. The CT of Randy's chest had shown a large mass—not in his lungs, but in the space between them, the area

called the mediastinum. A biopsy revealed the final diagnosis—Hodgkin’s lymphoma, a cancer that attacks the immune system. He had what is called a paraneoplastic syndrome, a rare complication in which antibodies to his cancer attacked the healthy cells in his brain.

Randy had surgery to reduce the size of the mass and then started chemotherapy. And slowly, remarkably, his memory began to improve. But the trip to New York remains vague, and his only memory of his weeklong hospital stay is his nurse telling him he was going home.

His fiancée remembers the day she realized he was getting better. It was several weeks after leaving the hospital. She reminded him that he wanted to get a haircut. He told her that he tried to go the day before but the line at the barbershop was too long.

She almost cried. “At that moment,” she told me, “I finally knew that the man I loved was still in there and that he was coming back.”

When I called Randy after receiving his e-mail, he still couldn’t remember much of his ordeal, but he understood the illness and the prognosis. One doctor stood out from the crowd of physicians caring for him. Marc Wein was a medical student at Brigham, and he had become fascinated by Randy and his illness. He read voraciously about the disease, tracked down case reports of other patients with a similar manifestation of cancer, and came back again and again to explain it all to Randy and Leslie. Together Marc and Randy created the story of this remarkable diagnosis that made sense to both of them. And that made all the difference.

Randy tells me he was never in pain but he hated the way he became a clean slate every five minutes. He hated the worried looks he saw on the faces of those he loved. He hated the loss of a sense of who he even was.

He embraced the story that Wein put together for him. Leslie had to remind him frequently of the particulars of that story, but he remembered that he had a cancer and that curing that cancer would restore him to himself. He welcomed the surgery and never minded the pain from the incision down his chest. He even looked forward to chemotherapy. Watching the intravenous needle pierce his skin, he remembered it meant he was one step closer to getting better. I spoke with Randy several times as he faced his

ordeal. His optimism never flagged. He is now disease free and his life has moved on. He returned to work five months after that strange weekend and got married the next year.

Randy's body may have been cured by the chemotherapy, but his mind was healed by a story.