

Unprotected People: #102 Hepatitis B

A Lost Week by Mary E. O'Brien, MD

The Immunization Action Coalition (IAC) publishes Unprotected People Reports about people who have suffered or died from vaccine-preventable diseases. This is the 102nd in our series.

Dr. Mary O'Brien, a physician at Columbia University Health Service, wrote this gripping piece about the rapid deterioration in health of her patient Thomas, a 25-year-old graduate student. O'Brien discovers that Thomas is suffering from acute hepatitis B infection. She explains the disease process from infection to fulminant liver failure. The article is lengthy, but the prose is vivid and the story is unrelenting. As you read about Thomas, remember that hepatitis B infection can be a very serious disease and one that is totally preventable with routine immunization.

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I am a doctor at Columbia University Health Service. Most of my patients are students who are young and healthy. The challenge is to stay alert to those who may be seriously ill. Thomas was one such patient. He came to see me on a morning when I had already evaluated several students with colds, one with a sprained ankle, a woman who had slipped on ice and broken her arm, and an employee with severe asthma.

Thomas is a twenty-five-year-old graduate student—tall and attractive, with short, stylishly tousled hair. He had written down "fatigue and nausea" as his complaint on the medical intake form. The intake nurse recorded that he had eaten pork recently and was wondering if he had food poisoning. His skin looked sallow, and, on close inspection, the whites of his eyes had a yellow tinge. He apologized for coming in with such nonspecific symptoms and was concerned that he was wasting my time, but, he ex-

plained, he just hadn't been himself.

Fatigue can be one of the toughest symptoms to sort out. Patients are frustrated that they have lost their normal energy level; they just want to feel better without answering a hundred questions. But since fatigue is present in almost all illnesses—the flu, heart disease, infections, cancer, as well as depression, stress, anxiety, too little sleep, too much work—it always takes careful questioning and a detailed history to figure out what is wrong and how to treat it.

I asked Thomas if he could go about his regular activities. No, he told me, he ran out of steam after the slightest exertion. A shower left him bone tired. It had taken him all morning just to get ready to come see me. He was constantly nauseated. Even the odor of food sickened him and could trigger vomiting.

I told him that his fatigue and queasiness, together with the development of jaundice, indicated a liver problem, probably hepatitis. But what kind of hepatitis, and how did he get it? Hepatitis is a general term referring to any illness that causes inflammation of the liver. Alcohol abuse, drugs or toxins, viruses like hepatitis A, B, and C, parasites, autoimmune diseases are all likely culprits. A patient's history often provides the answer even before the lab results are back. Thomas wasn't a drinker, and he didn't take any medications, herbs, or nutritional supplements. He reported no typical risk factors for hepatitis B, such as blood transfusions, surgery, and injection or skin-popping of illegal drugs.

"What about unprotected sex, any new partners?" I asked him. He frowned.

"Yes," he answered.

He had had unprotected sex with another man, but

(continued on next page)

that had been several weeks ago. Unfortunately, the most common route of transmission of hepatitis B in the United States is through unprotected sex. The incubation period between exposure to hepatitis B virus and the onset of clinical symptoms is several weeks, which fit his history perfectly.

I examined him carefully, searching for additional clues. Other than jaundice and mild tenderness over his liver, his physical exam was normal. Then I drew blood to evaluate his liver function and to determine whether hepatitis B was the cause.

We chatted a bit. Thomas told me that he had grown up in Switzerland and had learned English when he was eleven. I could barely detect an accent and congratulated him on his fluency. He laughed and told me he was a great imitator, and that is how he had lost his accent.

There is no specific medical treatment for hepatitis B, and usually patients can remain at home during their illness as long as they can keep down fluids and nourishment. I was quite concerned about Thomas's weakness and nausea, but he promised that he would arrange to have someone look in on him to make sure that he wasn't getting worse. We shook hands and said good-bye, and I told him that I would call the following day to see how he was feeling and to give him the results of his blood tests.

The liver is the workhorse of the human body, going about its myriad tasks with almost none of the credit or glamour associated with the heart or lungs. At two-and-a-half to three-and-a-half pounds, the liver is the largest organ in the body. It synthesizes most of the essential proteins that circulate in the blood, including albumin and coagulation proteins that clot blood, as well as many hormonal and growth factors.

The liver is involved in the metabolism of all the foods absorbed in the intestines. Nutrients are brought for processing from the intestines to the liver via the portal vein. They include glucose, which is converted to glycogen, its storage form; amino acids, which are the building blocks of proteins; fats that are stored as lipids; and cholesterol. The liver helps regulate these absorbed nutrients, releasing them into the blood stream when needed or converting them to storage forms for future use. The liver also

detoxifies drugs and other waste compounds in the body and prepares them for excretion.

Unfortunately, there are no specific blood tests to measure accurately the degree of liver damage, so I knew that I would have to estimate the severity of Thomas's illness by carefully monitoring his symptoms and performing physical exams and serial blood tests.

Early the next morning, Tuesday, January 13, I received the first batch of his blood tests, and my worries were confirmed. His bilirubin, a pigment formed from the breakdown of old red blood cells and normally excreted by the liver, was elevated. This caused his jaundice. The levels of two liver enzymes, AST and ALT, which leak out of damaged liver cells and into the blood, were staggeringly high at 6,000 and 8,000. (The normal range is less than forty.) But more worrisome was a doubling of his pro-time (PT), an indication that his liver was seriously damaged and could no longer synthesize blood-clotting proteins. It would take twice as long for his blood to clot. This impairment extended to all of the other essential proteins synthesized in the liver as well as to hepatic nutrient regulation and the liver's handling and detoxification of ammonia and other compounds. Such severe compromise of the liver is not commonly seen in acute hepatitis B. It can be a sign of impending liver failure.

I called Arthur Magun, an exceptional hepatologist at Columbia Presbyterian Hospital and an old friend from our days together as medical residents. He agreed that Thomas's lab tests indicated severe, acute hepatitis, most likely hepatitis B contracted from his recent sexual contact. Our main concern was whether or not to hospitalize him for supportive care and close observation of his liver function should it continue to deteriorate. I told Arthur that I would call the patient at home to find out how he was doing, and then we would make a decision.

When I reached Thomas, about midday on Tuesday, I didn't recognize his voice. It was barely audible.

"I just feel too weak to even eat," he said. "I threw up

(page 2 of 7)

twice and I can hardly get out of bed to get a drink of water. What's wrong with me?" I explained to him that he had severe hepatitis and asked him to have his roommate bring him to Columbia Presbyterian Emergency Department so he could be admitted to the hospital under Dr. Magun's care. I told him that I would speak to the doctors in the ER so they would be expecting him.

I have had little contact with the Presbyterian ER since my medical residency there in the late 1970s and was surprised not only that the ER phone number was unchanged but also that a familiar Jamaican voice answered the phone.

"Area A, adult ER. Can I help you?"

"Alkan?" I asked. "Is that really you?" I couldn't believe he was still working there. He had been one of my favorite people in the ER.

"This is Mary O'Brien. I was a medical resident there about twenty-five years ago." There was a pause.

"Dr. O'Brien, the really tall woman," he said. "Yeah, sure I remember you. How are you?"

"I'm fine. I have two sons who are nearly grown although they still keep me busy. What about you?"

"Oh, the family's good. We're fine."

We both laughed, and then he connected me to the attending physician. I gave him a brief rundown on Thomas and faxed him his medical record.

After I had finished seeing all of my patients that day, I pulled out Thomas's chart and looked through it, wondering whether there had been a missed opportunity to vaccinate him against hepatitis B, which would have prevented this life-threatening illness. Later that evening when my husband and I were cooking dinner, I told him about the case and how concerned I was and how frustrated that Thomas hadn't been vaccinated.

"He's been seen four times at the health service for complaints related to sexually transmitted diseases (STDs) during the past three years. He's obviously not practicing safe sex. So why didn't someone push him to get vaccinated? He's intelligent. Why didn't he know and ask to be immunized? It's tragic. Now he

may die from a totally preventable disease."

During that week of Thomas's illness, I mentioned his case to a couple of friends with whom I regularly play tennis. They had no idea how severe hepatitis B infection could be or that everyone should be vaccinated against it. I polled a few other nonmedical friends who were also unaware of the public health implications of hepatitis B and the effectiveness of preventive vaccination. I wondered why this information was not better known to the public, and why the news media didn't provide useful public health information like this rather than frivolous medical reporting on the latest diet fads or Botox treatments.

It is disturbing that most American health insurance companies don't cover the costs of hepatitis B immunization for adults. The result is that these critical vaccinations are often neglected at great cost to individual patients, like Thomas, as well as to the entire society. Columbia's student health insurance does not cover the cost of hepatitis B immunization. Remarkably, the New York City Department of Health, despite its limited budget, will provide hepatitis B immunization free to anyone at its neighborhood STD and HIV clinics, a measure of the importance a far-sighted health agency places on this crucial vaccination.

Hepatitis B is a totally preventable disease. Yet it is an enormous public health problem—approximately 400 million people are infected worldwide. It is a major cause of chronic hepatitis, cirrhosis, liver cancer, and is responsible for about one million deaths per year. In the United States, 300,000 new cases of acute hepatitis B are reported to the Centers for Disease Control and Prevention annually. Worldwide, the highest rates of infection with hepatitis B occur in Southeast Asia, China, and Africa, where more than half the population may be infected at some point during their lives, and many become chronic carriers.

Commonly, in these countries, hepatitis B is transmitted vertically from mother to child neonatally, thus spreading hepatitis B from one generation to

the next. These children become chronic carriers and reservoirs of infection in their community by transmitting it to their sexual partners and later to their offspring. However, if an infant receives hepatitis B vaccination at birth along with immune globulin, the rate of infection can be reduced drastically.

A universal immunization program in Taiwan, instituted in 1984, reduced the hepatitis B carrier rate in children from 10 percent to 0.9 percent over a ten-year period. A policy of universal immunization of infants against hepatitis B is in place now in eighty-five countries and should significantly reduce the disease in children. Since 1991 the United States has mandated universal vaccination of infants, universal screening of pregnant women, and post-exposure prophylaxis of infants born to infected mothers to prevent vertical transmission. Hepatitis B vaccination is now a routine pediatric vaccination in the United States. A recent review by the Centers for Disease Control (CDC) reported an 89 percent decrease in the incidence of hepatitis B in children under nineteen years old over the past twelve years since these policies have been implemented.

Hepatitis B is also transmitted through sexual contact (both homosexuals and heterosexuals, especially those with multiple partners), shared drug needles, or any blood contact. This horizontal route of transmission is the prevalent one in North America, Europe, and Australia and accounted for Thomas's infection.

There has not been a universal immunization program for adults, and so the rate of hepatitis B vaccination in these high-risk adult groups has remained low. Not surprisingly they are one of the few age groups that has experienced an increased incidence of hepatitis B.

On Wednesday, January 14, the rest of Thomas's blood tests came back. He was positive for acute hepatitis B and had mounted a huge immune response. It was probably his own vigorous immune response that was attacking and damaging his liver. I called Dr. Magun with these results, and he told me that Thomas's PT had doubled again in the past twenty-four hours, indicating further deterioration in his liver's ability to synthesize blood-clotting proteins

as well as the myriad of other proteins manufactured in the liver. He was now at much greater risk of significant bleeding. Nevertheless, Thomas remained alert without any evidence that his liver damage had begun to affect his brain.

When the liver is severely impaired or failing, ammonia and other toxins not handled by the damaged liver can accumulate in the brain. Changes in cerebral blood flow and swelling and increased pressure in the brain can occur, resulting in changes in mental function that range from mild confusion to coma and death. This potentially reversible deterioration in brain function is referred to as hepatic encephalopathy. Asterixis, sometimes called "liver flap," is an early sign of hepatic encephalopathy. It is easily elicited by asking the patient to hold his hands straight out in front of him as if he were stopping traffic. If asterixis is present there is a rhythmic, intermittent loss of muscle tone, and the hands drop then quickly resume their original position. This characteristic flapping was not yet present in Thomas, so we all sat tight, hoping his infection would turn the corner and the liver would begin healing and working again. If he didn't rally he faced acute fulminant liver failure, the dramatic abrupt destruction of a healthy liver, and his only alternative would be a liver transplant.

By Thursday, January 15, his PT had risen to ninety seconds, and he had become a little confused and had developed mild asterixis. He was close to meeting the criteria for acute fulminant liver failure. Dr. Magun transferred Thomas to the intensive care unit (ICU) and called in the liver transplant team to evaluate him. There was no way, short of a liver biopsy, to determine whether his liver damage was reversible or whether the liver cells had been destroyed and only a liver transplant could save his life. With a PT of ninety seconds and a high risk of bleeding, Thomas was not a candidate for a liver biopsy. Instead, it was decided that the ICU staff would monitor him closely and try to support him during the uncertain wait for a liver.

Normally, there is about a two-hundred-day waiting

(page 4 of 7)

period for a donated liver in New York City, but Thomas was moved to the top of the list because of his critical condition. He was not a candidate for a living liver transplant from his brother or parents, because it would take too long for the transplanted piece to enlarge and regenerate after transplant, and he had no liver function to sustain him in the interim.

Seventy-two hours had elapsed since I had first seen Thomas in the health service; he had gone from simple nausea, fatigue, and jaundice to total liver failure, with death likely unless a liver were found. I had never witnessed such a rapid deterioration of a patient with acute hepatitis B. Thomas is not much older than my two sons. I try to maintain a dispassionate, professional manner with my patients, but I could not help but see my own boys in Thomas's position. I despaired over my powerlessness while watching this young man fall closer and closer to death with no available medical intervention to reverse his liver damage, except a liver transplant.

There are only about 2,000 cases of fulminant liver failure in the United States each year. Usually, those suffering acute fulminant liver failure are otherwise healthy, unlike other patients with end-stage liver disease. Tylenol overdoses account for 40 percent of these cases, idiosyncratic drug reactions for about 13 percent of them, and viral hepatitis for about 12 percent. In about 20 percent of cases, the cause is indeterminate. Before the advent of liver transplants, only 10 to 20 percent of these patients survived. With a liver transplant about 80 percent of patients are alive one year after transplant.

I wanted to call Thomas's parents in Switzerland. I was sure they had no idea of the seriousness of their son's condition. Ordinarily, I would never contact a patient's family without the patient's express permission, but that was now impossible because at this stage Thomas was deeply confused. I spoke with his roommate to get a sense of whether Thomas would want his parents to know. His roommate told me that Thomas had been in touch daily with his parents since he had been hospitalized and was quite close to them. He gave me their phone number.

It was about midnight in Switzerland when I called.

The phone rang twice, and I heard a man's sleepy voice. I identified myself and explained that Thomas had gotten much worse, that his liver was failing, and he had been moved to the ICU to await a liver transplant.

"But we just spoke to him this morning. He sounded a little silly and vague, but he only has hepatitis right?"

There was a brief silence. Then his mother, who was also on the line, asked, "Are you trying to tell us that he is dangerously ill and that we should come there?"

"Yes," I answered. "That's exactly what I am saying. You should come immediately."

I hung up the phone and took the subway up to 168th Street to Presbyterian Hospital to visit Thomas. Besides seeing him and talking with his doctors, I wanted to broach the delicate subject of getting the names of his sexual partners so the New York City Department of Health could reach them and try to prevent the further spread of hepatitis B to other people.

When I entered his ICU cubicle, Thomas was sprawled catty-corner across the bed, lying on his side facing the wall. His long, slender body was neatly dressed in blue, windowpane-checked pajamas. Without the beeping monitors or IV hookup, he looked as if he could have been lounging in his dorm room. When I called his name, he turned to look at me and giggled. There was no hint of recognition. Not sure how to start a conversation with a desperately ill man I barely knew, I said stupidly, "Hi, how are you feeling?"

"Not bad," he said brightly. "I'm going home soon." And he giggled again. His jaundice had deepened since I had last seen him, but otherwise he looked unchanged.

"I spoke with your parents," I told him, "and they are coming to see you. They are worried about how sick you are."

He smiled vaguely and picked at his pajamas. Hepatic encephalopathy can manifest itself in many ways—as confusion, drowsiness, agitation, paranoia, or

delusions. It was particularly eerie that, in Thomas, it took the form of an uncharacteristic giddiness and lightheartedness, a blissful unawareness of his life-threatening illness.

I left to find the doctors on call in the ICU. I spoke to the intern and the liver fellow, a trainee in liver diseases. After they filled me in on his condition, I asked whether anyone had gotten the names of Thomas's sexual contacts before he became too confused to remember them. No one had, but the intern volunteered to talk to Thomas with me, and we set off for his room. His eyes were closed when we entered, but he turned and tittered and winked at us when we called his name.

"You know we're worried that the person who gave you hepatitis may also spread it to other people. We need to know his name," I began. He frowned and briefly looked serious and then snickered.

"Oh, my lover you mean?"

"Yes," we both answered, our pens poised.

"That's Paul Jones, yeah."

"But isn't he your roommate? Is he also your lover?"

"Yes, that's what I said, my roommate, my lover, my roommate," he laughed and sat up.

"Well, let's start with a first name." No response. He seemed puzzled and embarrassed that his brain couldn't answer such a simple question. He gripped his head between his hands and shook it back and forth as if he might physically shake loose a name from the fog of his confusion.

"Where did you meet him?" Nothing. "Where does he live?"

"In the west twenties, on that long block between Ninth and Tenth," he replied, clear as a bell, and gave us an exact address.

"How about his phone number? Has he called you? Is it in your cell phone?"

"Of course," he said, and he began crawling around the bed looking for his cell phone. It was a truly bizarre scene. Here was Thomas, deathly ill, with his silliness and giggling masking the severity of his encephalopathy. And here we were, the intern and

I, carrying on this conversation about roommates and lovers and cell phone numbers as if we were planning a rendezvous.

Thomas continued to deteriorate. When his parents arrived the next afternoon, Friday, January 16, he could no longer speak English. Instead, he greeted them by yelling French obscenities; there was no hint of recognition. On Friday evening he went into a coma and developed decerebrate posturing, a primitive neurological sign in which the body is rigidly extended, with the arms straight at the sides and turned inward at the shoulders, the hands in fists, and the legs straight out with the toes pointed. It is an indication of acute and widespread injury to the brain, and it signals a dire emergency, because if it is not reversed, the person will suffer irreparable brain damage and die.

Early Saturday morning, January 17, the transplant team swung into action. Three transplant surgeons, three anesthesiologists, and two nurses worked for six hours to transplant a healthy liver into Thomas. Miraculously, the national organ donor registry had found a suitable liver in time. Before surgery the senior transplant surgeon met with Thomas's parents and informed them of the huge risks attendant upon emergency liver transplant surgery, especially in a case like their son's.

First, his brain function was already severely compromised, and any further increase in pressure could cause brain death. While a person is under general anesthesia, it is especially hard to monitor and regulate intracranial pressure.

Second, his blood was not clotting, so the risk of major hemorrhage during or after surgery was substantial, despite the intravenous administration of clotting factors throughout the operation. Third, liver transplant surgery is enormously complex, requiring the hookup of three different blood supplies: the portal venous system, to bring all of the nutrients from the intestines to the liver for handling; the hepatic artery, to supply the liver cells themselves with oxygen and nutrients; and the hepatic venous system, to transport all of the liver's products into

(page 6 of 7)

the blood stream for delivery to the rest of the body. In addition the bile ducts and their connection to the small intestine must be attached, so bilirubin can be eliminated through the intestines and the bile salts can aid in the absorption of fats from the small intestine.

After removing his damaged liver, but before Thomas was fully hooked up to his new liver, the anesthesia team became responsible for all of the liver's functions, such as blood coagulation and maintaining normal glucose levels in the blood. Amazingly, the surgery was successful, and he lived.

When I went to visit Thomas a few days later, he was out of the surgical intensive care unit and was on the transplant floor. As I walked through the door, he smiled and said, "Dr. O'Brien, how nice to see you. Thanks for coming." He introduced me to his parents. His color was better; his face was alert. He looked like the student I had met eight long days ago at the Columbia University Health Service.

"I guess I'm lucky," he said.

"Yes," I answered. "Do you remember when I visited you last Thursday evening in the ICU?"

"No. The last thing I remember is seeing you last Monday and getting admitted to the hospital on Tuesday. The rest is blank."

We talked briefly about the past week, and I described his confusion and the devastating destruction of his liver. He seemed a little unsettled by this conversation, and it occurred to me how hard it must be for him to grasp the drama of the past week and his near brush with death when he remembered none of it. How could he appreciate the number of doctors and hospital staff who had worked around the clock to save his life? How could he know how worried and preoccupied with his illness I had been?

"Well, I got my IV out. I feel hungry again and I'm allowed to eat regular food today. Tomorrow I am going back to the OR so they can close up my belly. My new liver was too swollen from all of the fluids I got during surgery, so surgeons couldn't sew me up after my transplant. They're going to try again tomorrow."

I looked over at his parents, who were about my age, slender and tall like Thomas. I wasn't sure whether they knew their son was gay or how he had acquired hepatitis, but I could identify with them as parents dropping everything to fly over and be with their son when he was deathly ill. Our eyes met and welled with tears, and I felt their sheer gratitude and relief that their son had survived.

As I was leaving I told Thomas to call me if he needed anything. Several days later I e-mailed him, asking how he felt and reminding him to send me the names of his sexual contacts. A few days passed, and I received an e-mail from him with the names of his partners and a brief note telling me he was recovering well and would stop by to see me before he went home to Switzerland.

The next afternoon he knocked on my door, carrying roses in a lovely beige ceramic half vase. He had remembered how small my office was and thought the half vase would fit nicely on my desk. Considering that he had not even recognized me when I had visited him in the ICU prior to his operation, I was amazed at his recall of our first meeting. He asked me lots of questions about what he was like during his lost week. He seemed to be trying to figure out how, during those several days, he had gone from being a healthy twenty-five-year-old to nearly dying then waking up with a transplanted liver. I had witnessed it, so perhaps he wanted me to fill in this strange gap of time and help him come to terms with his liver transplant.

Ordinarily, prospective transplant patients have several months to prepare psychologically for surgery and to understand what is involved in a lifetime of post-transplant care and immunosuppressant medications. Thomas had simply awakened in the hospital after transplant surgery, with no recall of the previous several days, to find his abdomen cut open and a new swollen liver protruding. We talked until my secretary's voice came over the intercom, announcing that my next patient had a fever and was waiting to be seen.

(page 7 of 7)