DIAGNOSTIC DEMONS

TAKING ON THE MOST CONFOUNDING CASES

By Mary Loftus

Emory Special Diagnostic Services, first patient, Sept. 30, 2013: *A 65-year-old man being evaluated for a renal transplant was referred by the transplant team for a workup. The reason for the referral was unusual lesions on his CT scan, multiple pulmonary nodules, and abdominal lymphadenopathy. Biopsy result was sarcoidosis, a poorly understood disease.*

Nearly three years after seeing their first patient, the Emory Special Diagnostic Services team is sitting around a long table in a conference room on the first floor of the Emory Clinic, discussing challenging cases.

"It's what inspires us, what we love," says Special Diagnostic Services director Clyde Partin.

The team, consisting of five doctors and one nurse navigator, holds these roundtables routinely. "It's always helpful to have more than one brain considering a patient's case," says Tom Jarrett, an internist at Emory Clinic. "We go in open-minded to all possibilities."

Emory Special Diagnostic Services, part of the Paul W. Seavey Comprehensive Internal Medicine Clinic, is one of a handful of such clinics around the country, dedicated to patients with complex, undiagnosed illnesses. The team has seen more than 200 patients since opening, about half of whom received diagnoses. "What people really want is an answer," says Partin, who is sometimes called "Emory's Dr. House" for his diagnostic acumen, a moniker that, while tongue-in-cheek, is not far off the mark.

CASE STUDY 1: A photo of a middle-aged school teacher showed up on Dr. Clyde Partin's cell phone. The patient was requesting a consult. "Swollen face" was the complaint. Her neck was erythematous with a red rash, Partin observed, and she appeared tired. Upon her arrival at the special diagnostic clinic, Partin encountered a 45-year-old woman, slightly overweight. She showed him a different photo of herself taken at a party, her face thin and youthful, just five months previous. She told him that she was exhausted, had gained twenty pounds, and could hardly climb up steps. Her past medical history included migraine headaches, which were worsening, and neck and back pain—for which she had had epidural steroid shots, 10 shots in the past 13 months. Diagnosis: excessive exogenous steroids, producing Cushing syndrome and steroid myopathy.

"A DISEASE KNOWN IS HALF-CURED." —proverb attributed to physician-preacher **Thomas Fuller**, who died of typhus in 1661

CASE STUDY 2: Drew Crenshaw was 18 when he started having severe ankle pain. An X-ray showed the college freshman had minor stress fractures in both feet. Casts were placed on his feet, and Crenshaw was wheelchair-bound for six months. He withdrew from college in Florida and retreated to his home. But the pain continued even after the casts were removed, and then he developed pain in all of his joints. "Some days, the pain was so bad I could not even get out of bed," says Crenshaw. "My shoulders, knees, elbows, fingers and ankles were all affected. Everything hurt." After multiple visits to doctors and health care facilities in several states, Crenshaw ended up at Emory's Special Diagnostic clinic, where doctors determined that he had a severe case of gout, a condition often characterized by recurrent attacks of severe inflammatory arthritis. "With a diagnosis confirmed, the team ordered specific medications for Drew while getting all of his biochemical levels back in balance," says Debra Cohen, nurse navigator.

To prepare for the Special Diagnostic clinic's opening, Partin and his team of Rollins Distinguished Clinicians reviewed diagnoses of *House MD* scripts from the long-running Fox series and analyzed Lisa Sanders's "Diagnosis" and "Think Like a Doctor" columns from *The New York Times*, many of which served as the basis for *House* episodes. They also reviewed the *New England Journal of Medicine's* first 200 case conferences from the 1920s as well as 200 modern cases from 2005 to 2007.

"It may not have been the most scientific approach, but we were curious about what sort of diagnoses were persistently perplexing," Partin says.

His own preparations included reading up on commonly missed diagnoses in outpatient settings, although he found the literature on this to be sparse and more focused on inpatient diagnoses.

"The subtle distinctions between missed diagnoses versus misdiagnoses can be vexing," he says. "Atypical presentations of common diseases are much more likely than typical presentations of rare disease. "

In other words, the medical adage, "When you hear hoofbeats, think horses, not zebras," holds true even for diagnostic clinics.

For each referred patient, the team requests existing medical records, imaging, and letters from previous doctors; takes a thorough medical and family history; and conducts a comprehensive physical examination, often with a variety of tests, new imaging, and tissue biopsies. Depending on the findings, Emory specialists from neurology to genetics are consulted.

"A lot of times, we know what it's not, but not what it is," says clinic internist Sharon Bergquist. Some of the seemingly mysterious cases brought before them are "just oversights from disjointed evaluations," she adds. "We take a second look to make sure that all elements of the patient's history are taken into consideration."

Often, even before coming to the clinic, the patients have seen multiple doctors and researched all of the horrible diseases that could possibly be related to their symptoms, courtesy of Google.

But symptoms, as Partin is fond of saying, do not a diagnosis make.

Unlike the patient cases handpicked for TV medical dramas, which are almost always neatly wrapped up by the end of the hour, "in the trenches of diagnostic clinics, answers waltz out of the closet less than half the time," he says. "That is one of the unfortunate realities of seeing the most difficult cases. There has to be a realistic willingness to accept failure."

The most common of the clinic's 100-plus diagnoses so far were neurologic (17), followed by circulatory, digestive, and musculoskeletal. There were nine mental health diagnoses. Eight patients died.

The clinic's team—including Partin, Jarrett, Bergquist, David Roberts, and Jonathan Masor, along with nurse-navigator Debra Cohen—have developed their own intriguing case files, some of which can be read in the regular "You Be the Doctor" column in this magazine.

Physicians who specialize in such difficult-to-diagnose cases are sometimes called "disease detectives"— modern, medical Sherlock Holmeses. In fact, one of the defining books in the field is the late *New Yorker* writer Berton Roueche's 1947 nonfiction collection, *The Medical Detectives*, based in large part on his "Annals of Medicine" column.

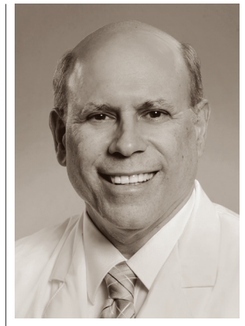
Diagnostic Overload

- Practicing physicians draw on a store of at least 2 million facts
- Google can access > 3 billion articles
- Physicians process about 236 bits of data during an ICU visit
- WHO lists 12,420 distinct disease categories
- About 7,000 rare diseases exist; about 400 have prescribed treatments

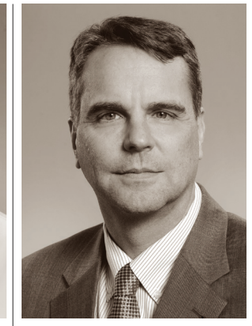
Sharon Bergquist, assistant professor of medicine, internist.

Debra Cohen, nurse navigator.

Thomas Jarrett, assistant professor of medicine, internist.



Jonathan Masor, associate professor of medicine, internist.



David Roberts, Charles F. Evans Professor of Medicine, internist.

But Partin sees other less obvious comparisons as well, such as the Magliozzi brothers, Tom and Ray, of *Car Talk* radio fame. "They were a brilliant example of deductive reasoning leading to a solid diagnosis time after time," he says.

And so, the perfect diagnostician: part intuitive clinician, part mythical detective, part auto mechanic.

The generous time and resources that often must be devoted to complex patient cases may seem antithetical to the current emphasis on productivity related to the economic squeeze on health care providers. Indeed, many special diagnostic clinics—like Emory's, which is funded largely through a grant from the O. Wayne Rollins Foundation—must rely on private philanthropy.

"The special diagnostic clinic was developed to meet what we thought was an unmet national need," says Doug Morris, former director of the Emory Clinic and a driving force behind the diagnostic clinic. "In spite of enormous technological advances, there remains a multitude of patients who suffer the torment of undiagnosed or misdiagnosed disease."

While the special diagnostic team is largely made up of internal medicine and primary care physicians—generalists, who take a comprehensive view—there's a reason such clinics are often housed in academic medical centers: a host of specialists are needed to consult on cases, including neurologists, pathologists, geneticists, gastroenterologists, cardiologists, infectious disease doctors, rheumatologists, and psychiatrists. "There's a great tension between what is psychosomatic and what is organic," says Partin, who recently attended an international conference on rare diseases and undiagnosed illnesses in Vienna, and toured Freud's home and office.

Modern diagnostic clinics rely on advanced imaging, pathology lab results ("The issue is tissue," Partin often says), and, more and more frequently, genetic testing, allowing doctors to investigate the possibility that a puzzling illness or set of symptoms is caused by an inherited condition or genetic mutation.

Partin believes that computer analysis and genome sequencing will play larger roles in difficult diagnoses in the future.

But the knowledge and intuition of experienced doctors and specialists, above and beyond their tools and technologies, cannot be overstated. Of the Emory Special Diagnostic clinic's resolved cases, 17 were diagnosed through biochemical/lab results, 21 through pathology, 12 through radiology, 2 through response to treatment—and 58 through "clinical acumen."

Even when a diagnosis is made, however, it can be hard to determine the best point at which to stop the inquiry. Partin prefers to seek out root causes. "The best thing you can do is keep asking yourself why. Something as simple as a patient with abdominal pain, is it due to pancreatitis? Why do they have pancreatitis? The gallstones. Why do they have gallstones?" says Partin. "You can go to the nth degree, and sometimes you will strike gold and sometimes you will hit a metaphysical dead end."

A year after a patient visits the clinic, the staff contacts them to check on the validity of the diagnosis. Emory's diagnostic clinic has had many gratifying successes—patients whose illnesses were identified and then properly treated. The team has diagnosed Lyme disease, post-polio syndrome, anemia, West Nile virus, sleep apnea, endometriosis, depression, neurodegenerative diseases, conversion disorders, and dozens of other common and rare conditions.

CASE STUDY 3: The 59-year-old female patient was experiencing shortness of breath, especially after physical effort like climbing steps. She had fatigue and left pleuritic-type chest pain, as well as tachycardia. She had been a smoker but quit in 1983. Her stress echocardiogram was normal, as was a chest CT scan and bronchoscopy. When the doctors asked if she snored, the answer was a resounding yes. Diagnosis? Moderately severe sleep apnea. With the use of a CPAP, she experienced complete resolution of her symptoms.

Claiming victory with a definitive diagnosis, however, remains a tricky business. "Are we 100-percent right? There is a murky middle ground that makes us feel like our feet are firmly planted in mid-air," Partin says. "So any case we do unequivocally solve is a cherished triumph." ■