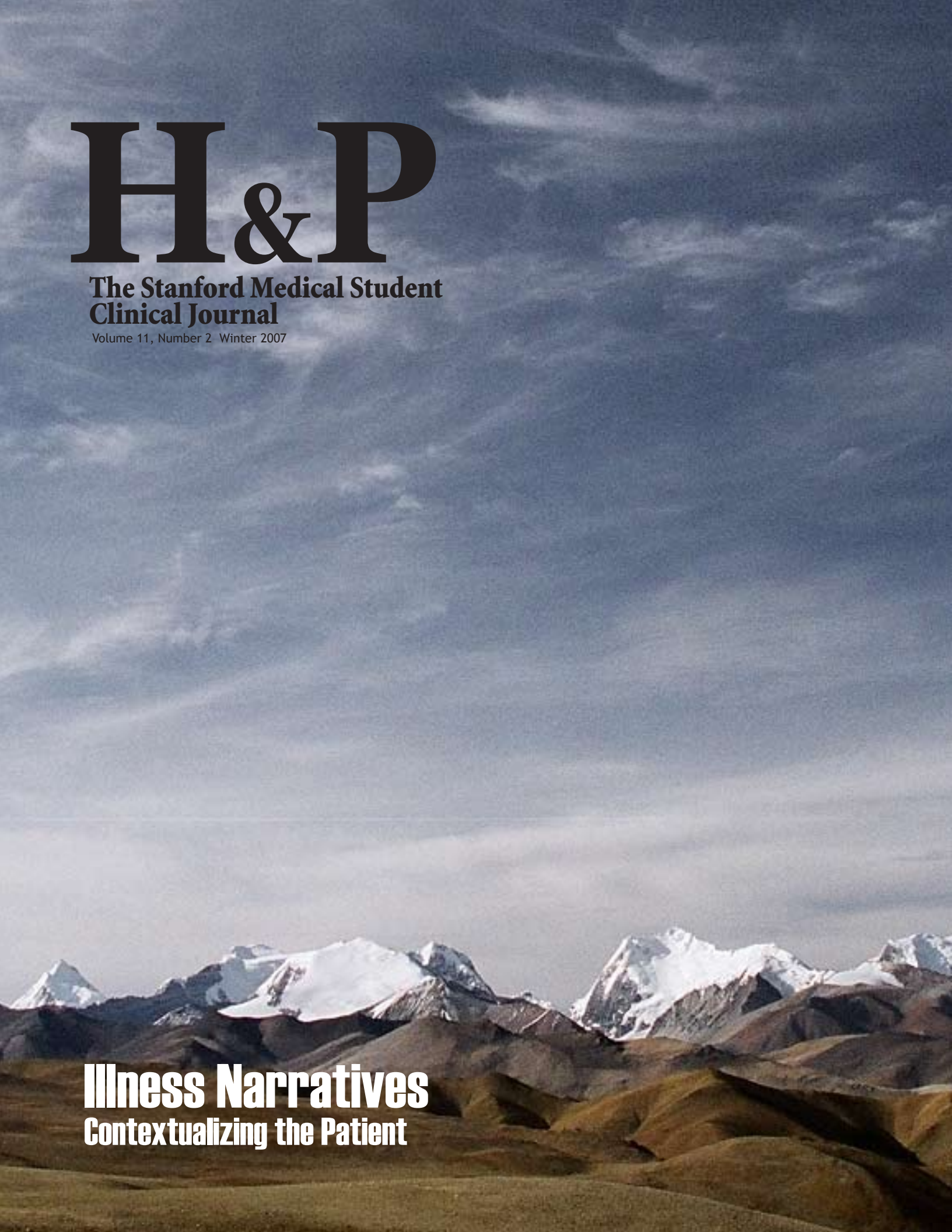

H&P

The Stanford Medical Student Clinical Journal

Volume 11, Number 2 Winter 2007

Illness Narratives

Contextualizing the Patient

Contents

H&P
The Stanford Medical Student Clinical Journal

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Editors' Note

Becoming a doctor involves learning a new language. After four years filled with coursework and clinical rotations, we emerge with an understanding of medical knowledge and a newfound fluency in medical speak. "Touch" becomes "palpate," and "heart attack" becomes "myocardial infarct." We learn how to interpret cryptic acronyms like PERRLA, HEENT, BUN, SLE. One of the most important aspects of this process is learning to employ our medico-linguistic skills as we write up (or dictate) a clinical report. The purpose of a clinical report is to categorize and quantify illness, so that each particular patient is reduced to a series of signs, symptoms, and physical findings. We can use these findings to help us decide upon a diagnosis and treatment plan for our patient.

Over the course of our medical training we become more and more adept at the process of translating a patient's experience into the language of medicine. We learn how to streamline the interview by only asking questions that are most relevant to the patient's particular illness. We shorten the physical exam by only examining the parts of the body that are absolutely necessary in order to reach a secure diagnosis. At the same time we often forget that the woman in room 237a is much more than a case of community-acquired pneumonia. She is first and foremost a *unique individual*, a grandmother who enjoys taking a daily walk with her black Labrador and is looking forward to her youngest grandson's birthday next week.

The irony is that most of us chose medicine as a career because of a desire to interact with others in a truly meaningful manner, but once we start rotations in the hospital, we feel stressed and overworked, and our patients become cranky and uncooperative. Kindness and empathy no longer seem as important to us as signing out and getting a good night of sleep.

The question then emerges: How do we prevent ourselves from looking into room 237a and seeing just another problem list and differential diagnosis in need of lab tests and imaging studies? How do we maintain the sense of awe that brought us into medicine in the first place?

One answer is through writing. We can put down the medico-linguistic pen that we use to compose our clinical case report and pick up the creative writing pen. We can ask our patients questions that do not relate to their illness. Such questions allow us to connect with our patients on a personal level and thus bring back the empathy that is so important in medicine. Furthermore, by sitting down for a few minutes at the end of the day and putting words on paper we engage in a process of self-reflection that forces us to remember how each patient is unique; we remember the little jokes, the difficult conversations, the eager smiles, the painful stares, and even the flowing tears.

Our second issue of H&P highlights the role of patient narratives in medicine. In addition to our usual clinical case reports, we present personal stories from four medical students who each share with us the tale of a patient told not through the clinical detail of a medical report but rather through the compassion and creativity of a narrative. Kristen Whitaker tells of her experience performing narrative therapy with a bright teenage girl with diabetes. Jenya Kaufman writes about a schizophrenic patient who refused her care. Ashley Plant shares her experiences interacting with a beautiful child who "failed to thrive." Dona Tversky tells the story of a young father who suffers a stroke. To complement these essays by medical students, we also present an illness narrative written by a patient herself. Ginger Vieira, the teen featured in Kristen Whitaker's essay, has agreed to share with us a piece of her own writing.

The medical narratives featured in this issue of H&P are demonstrations of the power of language to refocus the doctor-patient interaction in terms of emotion rather than objectivity. At the same time, we, as editors of the student journal, realize that openly publishing such personal accounts can potentially violate the sacred trust that patients place in medical professionals. So we have ensured that the patients featured in these narratives have granted us permission to tell their stories.

In our Literary Arts section we continue with our theme by presenting an interview with Dr. Michael Marmor, who helped start the "Medicine and the Arts Program" which was recently integrated into the Practice of Medicine Class. As an introduction to the Medicine and the Arts Program, the entire first year medical student class recently attended a performance of *The Imaginary Invalid* by Moliere. Chantal Forfota, our *H&P* Literary Arts editor, writes in this issue about the portrayal of the medical profession in Moliere's play. Also in our Literary Arts section we present a poem by Christina Chao, a painting by Jacqueline Ng, and a humorous reflection on lab work by Steve Minear.

On the scientific front, this issue features a profile of Achal Achrol's research on arterio-venous malformations and an overview of the medical implications of population genetics by Amanda Casto. Our clinical case reports highlight the management of mucormycosis and bezoar, and in our ethics report Steven Lin ponders the issues involved in determining whether to give organ transplants to mentally retarded children.

Picasso once painted a curious portrait of a man with one eye open and one eye closed—the sitter might as well have been a medical student. We need to keep one eye closed to maintain our professional objectivity and distance, yet we need to keep that other eye open to be able to see the patient as an individual and not a disease. We challenge our readers to consider making narrative medicine an aspect of your own medical practice. Take a few minutes to forget about the science of medicine and instead exercise the art. Sing a song, draw a picture, tell a story; just make sure that both eyes are not closed.

James Colbert
Thomas Tsai

CLINICAL CASE REPORT

Not Just Acute Sinusitis: Invasive Rhinocerebral Mucormycosis

Daniel R. Sanchez and Marina Martin, M.D.

ABSTRACT

Rhinocerebral mucormycosis is a rapidly progressive, life-threatening infection that almost always occurs in patients with diabetes mellitus, leukemia, lymphoma, or immunosuppression. The patient presented in this case report is typical of those most vulnerable. A 77-year-old diabetic man on chemotherapy for chronic lymphocytic leukemia presented with left-sided maxillary edema, erythema, and numbness, along with ptosis of the left eye and paralysis of the lower left half of the face. The patient was admitted to the hospital for administration of broad-spectrum intravenous antibiotics and voriconazole, and his signs and symptoms improved rapidly. Sinus fluid specimens and a nasopharyngeal biopsy were subsequently positive for Mucor, and he was started on amphotericin B. After the patient and medical team weighed the risks and benefits of aggressive surgical debridement and decided against it, he ultimately continued amphotericin B as an outpatient. This report discusses the pathogenesis, clinical presentation, diagnostic workup, and management of mucormycosis and underscores the importance of prompt diagnosis in providing the optimal chance for a cure.

INTRODUCTION

Rhinocerebral mucormycosis is a rapidly progressive, life-threatening infection that almost always occurs in patients with diabetes mellitus, leukemia, lymphoma, or immunosuppression.[1-5] Recognizing patients at risk, in addition to understanding the presentation of the disease, is of paramount importance, because prompt diagnosis is critical in providing the optimal chance for a cure.[1,2,4] The index of suspicion must be high, since a biopsy and specially-prepared culture are standard for diagnosis.[1,3,4] Although surgical debridement is the mainstay of management for mucormycosis,[1,3,4] this may not be appropriate for all patients.

CASE REPORT

A 77-year-old diabetic man with a history of chronic lymphocytic leukemia (CLL) and Richter's transformation to large B-cell lymphoma was undergoing chemotherapy when he developed a productive cough and rhinorrhea. He received a ten-day course of oral ciprofloxacin as an outpatient, and his chemotherapy was held. Over the next three weeks his symptoms progressed, and he was admitted for fever, sinus tenderness, and evidence of bilateral maxillary sinusitis on x-ray. At admission, his absolute neutrophil count (ANC) was 1078 (reference: 1800-9130). The patient was treated with broad-spectrum IV antibiotics and voriconazole before being discharged on oral antibiotics and the voriconazole. Over the next three days the patient developed fever to 101.5 degrees Fahrenheit, along with swelling, redness, and numbness of the left cheek. He also noticed facial drooping in the left eyelid and mouth, which had occurred once previously many years ago. On review of symptoms he endorsed cough, nasal congestion, and white nasal mucous discharge for many weeks but denied blurry vision or vision loss, dysphagia, ear pain, hearing loss, or headache. On the day of admission the patient was seen in hematology clinic and immediately sent to otolaryngology (ENT) clinic for evaluation. An otolaryngologist penetrated and irrigated the patient's left maxillary sinus via rigid endoscopy. Although polypoid changes were found, no pus was discovered.

On physical examination, the patient was febrile to 100.8 degrees Fahrenheit, but other vital signs were normal. In general he was well-nourished, alert and oriented to person, place, and time, and in no apparent distress. He had ptosis of the left eye, a left-sided facial droop, and erythema, edema, and numbness of the left maxillary area. His pupils were equally round and reactive to light and his oropharynx and nasal passages were unremarkable. The rest of his examination was normal.

A complete blood count revealed a white blood cell count of 4.3 K/µL (reference: 4.5-11.0 K/µL), with an ANC of 2537 consisting of 13 percent bands (reference: 0-4 percent), a hemoglobin of 11.1 g/dL (reference: 14.0-17.0 g/dL), and a hematocrit of 31.3% (reference: 39.0-51.0 percent). A basic metabolic panel was normal except for glucose of 191 mg/dL (reference: 70-100 mg/dL) and albumin of 3.0 g/dL (reference: 3.2-5.0 g/dL). A hemoglobin A1c was 6.4 percent (reference: 4.0-6.0 percent). A facial MRI showed soft-tissue swelling and

abnormal enhancement of the left face with severe bilateral maxillary and ethmoid sinusitis (Figure 1). There was also possible spread to the preseptal space of the left lateral orbit and left pterygopalatine fossa.

The patient was admitted for administration of broad spectrum antibiotics and antifungal agents. He was empirically started on IV meropenem and IV voriconazole alongside frequent neurological examinations. The left maxillary erythema and edema resolved rapidly, and there was mild improvement in the left-sided ptosis and facial droop. A maxillary sinus endoscopy and partial ethmoidectomy were performed four days after admission, and although a "fungus ball" was noted, no necrosis was seen. However, the nasal fluid specimen subsequently grew *Mucor* species, and a nasopharyngeal biopsy was positive for invasive *Mucor* (Figure 2). The patient was immediately switched to amphotericin B monotherapy. A follow-up MRI showed no evidence of intracranial extension, though it suggested to the ENT team that surgical resection would require radical disfigurement and excessive morbidity. After the multidisciplinary team weighed the risks and benefits of surgical intervention in extensive discussions with the patient and his family, the patient elected outpatient amphotericin B treatment instead of surgery. He was discharged eleven days after admission with almost complete resolution of his signs and symptoms.

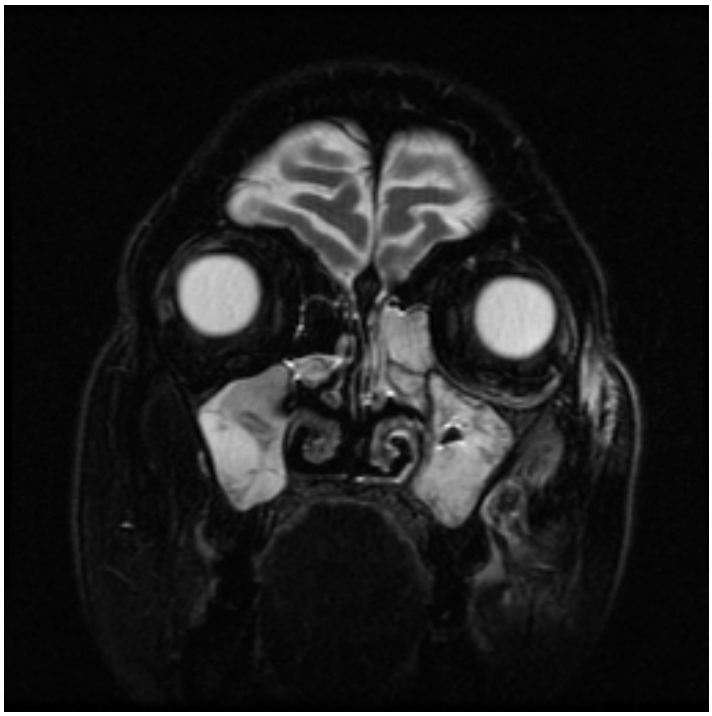

Figure 1. Coronal T2-weighted FSE MRI of patient demonstrating bilateral maxillary and ethmoid sinusitis.

DISCUSSION

Mucormycosis, also referred to as zygomycosis based on a more general taxonomic classification, is caused by an ubiquitous fungus commonly found on decaying matter such as fruit and bread.[1] Rhinocerebral infection, the most common presentation of mucormycosis, occurs via the inhalation of spores, a process which occurs in nearly all humans every day.[2] However, in the normal host, macrophages will contain the spores through a phagocytic response.[3] If this response fails, germination will occur and hyphae will develop.[4]

The patient presented in this case report is typical of those most vulnerable to the development of rhinocerebral mucormycosis. Since neutrophils are responsible for clearing fungal hyphae, infection almost always occurs in poorly-controlled diabetic (especially when in diabetic ketoacidosis) or immunocompromised patients. Members of the former group have impaired neutrophil function (via the high glucose/low serum pH environment) while those of the latter have decreased numbers of neutrophils.[1-3] The use of voriconazole has also been implicated in mucormycosis development, presumably through selective pressure for growth.[3]

Rhinocerebral mucormycosis presents like acute sinusitis with fever, sinus pain, and purulent nasal discharge. Invasive mucormycosis may also produce facial swelling, vision disturbances, and mental status changes, as it usually spreads rapidly to involve all of the sinuses and adjacent structures such as the palate, orbit, and brain. As hyphae invade the vasculature, adjacent tissues infarct and subsequently undergo necrosis, resulting in black eschars on the palate, septum, or turbinates - a hallmark of the disease.[1,3] Infarction of branches of the fifth cranial nerve may cause facial numbness, as demonstrated in this patient.

Rapid diagnosis and treatment are the most important factors in increasing survival rates from invasive mucormycosis. In a relatively large metanalysis it was found that the survival rate from rhino-orbital-cerebral mucormycosis begins to decline when the interval from onset of first symptoms to treatment is longer than six days. As the interval to amphotericin B treatment increased from one to six days to seven to twelve days, survival rates fell from 76 percent to 35 percent. Similarly, as the interval to surgery increased from one to six days to 13 to 30 days, survival rates fell from 81 percent to 42 percent.[4]

Although sinus fluid cultures may be helpful, they are often negative. The diagnosis is made from biopsy or specialized culture, requiring clinicians to highly suspect mucormycosis for prompt diagnosis. Since the fragile mucor hyphae are usually destroyed during the grinding of specimens, the laboratory must be informed of the presumptive diagnosis so as to finely mince the tissue for culture instead.[1,3,4]

Treatment includes reversing any metabolic disturbances (e.g., ketoacidosis) as well as reversing immunosuppression. While high-dose amphotericin B is the drug of choice, recent studies have shown promise for posaconazole, a novel triazole, in treating mucormycosis refractory to amphotericin B.[3,5] However, all medical management is merely adjunctive to surgical intervention. Aggressive surgical debridement, often repeatedly required, is the current mainstay of therapy.[1,3,4]

As was demonstrated in this case, the risks and benefits of radical surgery must be carefully evaluated. This patient would have required extensive debridement and a lengthy, if not uncertain, recovery process. Overall, the prognosis for recovery from mucormycosis is poor with a mortality rate of

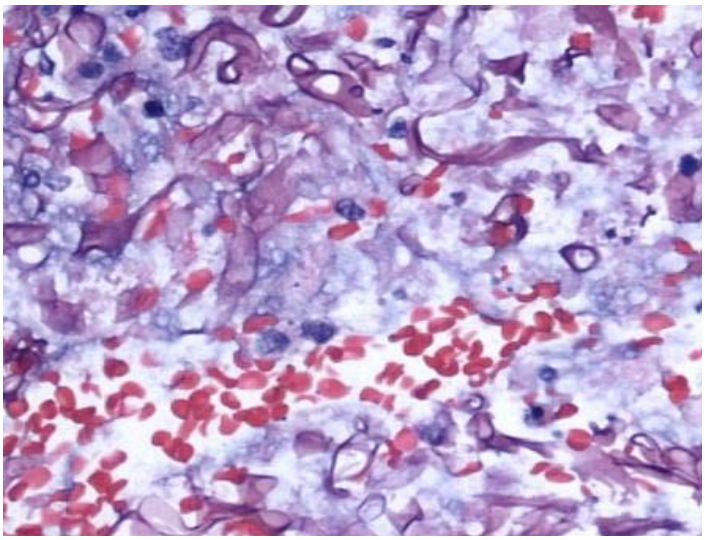

Figure 2. Nasopharyngeal biopsy from patient demonstrating angioinvasive mucormycosis. Mucor hyphae are broad and nonseptate, with perpendicular branching patterns.

50-80 percent.[1,2] Further complicating this patient's decision algorithm was his diagnosis of CLL with Richter's transformation, an illness that in and of itself has a median survival of five to eight months.[6] Given the patient's satisfaction with his quality of life and the poor hematologic prognosis, our recommendation was to continue medical management as an outpatient.

In conclusion, diabetic or immunocompromised patients presenting with symptoms of sinusitis or acute vision disturbances should be carefully evaluated for mucormycosis. Prompt diagnosis and treatment is paramount in providing the optimal chance for a cure. In this case, a multidisciplinary collaboration between the hematology, infectious disease, and ENT teams was critical for developing appropriate treatment recommendations. Ultimately, however, it was the patient's wishes that dictated the plan of treatment.

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Graham Walker

CLINICAL CASE REPORT

Multiple Gastric and Intestinal Trichobezoars in a Nine-Year Old Girl

Joanna E. Wrede

ABSTRACT

Trichobezoars are conglomerates of hair in the gastrointestinal tract. They are common in children and adolescents and are more prevalent in girls than boys. An occasional complication is mechanical obstruction, usually at the gastric level or in the small bowel. In this case, a nine year-old female patient was admitted with abdominal pain and emesis. The patient endorsed a distant history of trichophagia two years prior. Imaging studies indicated small bowel obstruction with potential bezoars located in the stomach and small bowel. Endoscopy and laparotomy were performed identifying one trichobezoar in the stomach and four in the jejunum. The bezoars were extracted by enterotomy and gastrotomy. No post-operatory complications occurred. Other treatment options explored in the literature are discussed in this report. Since bezoars are rare entities that may be complicated by bowel obstruction and even perforation, it is useful to consider them in the differential of any bowel obstruction of unknown origin.

INTRODUCTION

The term "bezoar" refers to a conglomeration of undigested materials which forms a mass in the gastrointestinal tract. This word is derived from the Arabic "bazahr" or the Persian "padzahr," which literally mean "protection from poison." Animal bezoars were once highly valued as they were believed to act as a universal antidote against any poison. They were worn as charms and were believed to have magical properties.[1]

These accumulations most commonly consist of hair (trichobezoar) or plant material (phytobezoar), but bezoars consisting of drugs, food boluses, chewing gum,[2] and even such foreign bodies as doll's heads have been reported.[3,4]

Trichobezoars are most often located in the stomach, although they have also been found in the esophagus and small and large intestines.[5] Trichobezoars may be associated with trichotillomania (the abnormal desire to pull out one's hair) and trichophagia (the eating of hair). An occasional complication is mechanical obstruction, usually at the gastric level or in the small bowel. It is extremely rare to find trichobezoars in the small bowel without a gastric component. Presented here is a case of multiple trichobezoars in a young girl, involving both stomach and small bowel, followed by a discussion of typical presentation and treatment options for trichobezoars.

CASE REPORT

A previously healthy nine-year-old girl presented with a four day history of abdominal pain and subsequent emesis. Emesis on the day of admission was first bilious with the presence of hair, and then brown and hemoccult positive. Her last stool had occurred one day prior to admission. At presentation she experienced burning in the throat. According to her parents, the patient had a history of eating her own hair, but had stopped this behavior two years prior. They described her chewing on her long hair while it was still attached to her scalp. Of note was an incident three years prior in which she passed hair in her stool. The patient denied any recent pulling or chewing of her hair. She stated she was not very nervous, but her parents reported that she does get anxious easily and has a nervous habit of cracking her knuckles. There was no history of sick contacts, cough, diarrhea, fever, night sweats, weight change, or shortness of breath. She had no past surgical history and was taking no medications. There was no family history of medical or psychiatric problems. The patient's developmental history was normal. She was in fourth grade, doing very well in school. Her parents commented that she plays with her friends often and is quite intelligent.

Her initial vital signs included a temperature of 99.4 degrees Fahrenheit, heart rate of 112 beats per minute, blood pressure of 105/73 mmHg, and respirations of 22 per minute.

On physical examination, the patient was well developed, well nourished, alert, non-toxic, and in mild to moderate discomfort. Mucous membranes were slightly dry. She had shoulder-length hair, and no areas of alopecia were seen. Her abdomen was minimally distended with firmness over the left upper quadrant. Palpation illicited moderate tenderness in the epigastrium and mild diffuse tenderness throughout the abdomen. Voluntary guarding was noted during the examination. Bowel sounds were present. There were no masses, hepatosplenomegaly, rebound tenderness, ascites, or hernia. Abdominal x-rays showed a distended small bowel with air fluid levels (absent on later pre-operative films), gas in the colon and rectum, and changes in bowel gas patterns over

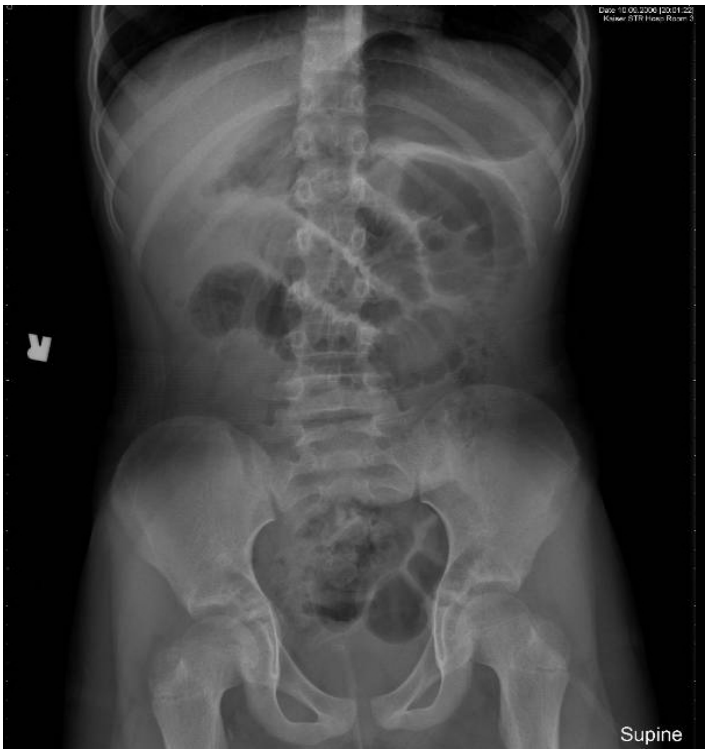

Figure 1. Abdominal radiograph, AP view, supine, with significant small bowel and gastric distension and thickened small bowel wall, consistent with small bowel obstruction

twelve hours consistent with partial small bowel obstruction (Figure 1). An abdominal CT scan was also consistent with partial small bowel obstruction; gastric contents noted on CT were consistent with a bezoar, and evidence of a bezoar was also seen in the mid-jejunal region. No abscess nor evidence of perforated appendix were noted. Her sodium was slightly low at 134 mEq/L (reference: 135-145 mEq/L). Otherwise an electrolyte panel, a complete blood count, and liver function tests were normal.

Our initial assessment was that the patient had a partial small bowel obstruction due to a trichobezoar. She was restricted to nothing by mouth and treated with intravenous fluids, a nasogastric tube to suction, and Phenergan suppositories for emesis control. A trial of Gastrografin was administered to delineate the site of small bowel obstruction and potentially mobilize the small bowel bezoar if one existed. When no change was seen in degree of small bowel obstruction, the patient was brought to the operating room for endoscopic and possible surgical intervention.

The procedure began with esophagogastroduodenoscopy. Under general anesthesia in the supine position, a GIF 160 Olympus endoscope was inserted through the mouth and carefully advanced to the third portion of the duodenum. The endoscope was slowly withdrawn and the mucosa was inspected. The findings were esophagitis and gastric bezoar. Additional duodenal bezoar was seen after laparotomy and milking of a small bowel bezoar toward the stomach (Figure 2). The gastric bezoar was grasped but was unable to be pulled through the gastroesophageal junction due to its large size. Jejunostomy and gastrotomy were performed next, removing one gastric and four jejunal bezoars. The jejunum at the point of the most distal bezoar did not appear to have any extrinsic or intrinsic narrowing. The stomach and bowel were inspected carefully to the point of the ileocecal valve and revealed no evidence of perforation or residual bezoar. The bezoars were bilious in color, fibrous, and ovoid. The gastric bezoar measured 2.5 cm in diameter by 11 cm in length, while the intestinal bezoars each measured 4 to 5 cm in maximum dimension.

The patient recovered without complication and received outpatient psychiatric follow-up.

DISCUSSION

The patient discussed in this case shares some common features with the majority of patients with trichobezoars reported in the literature. Trichobezoars are most frequently reported in children and adolescents, and 90 percent of the patients are girls under 20 years old.[6] Trichobezoars are predominately associated with trichotillomania, a habit of chronic hair pulling that is generally secondary to pica, mental retardation, or psychiatric disorders.[7] It is estimated that five to 18 percent of patients with trichotillomania eat their hair, with only a small number of those forming clinically significant trichobezoars.[8] Of question in this case is whether the patient had true trichotillomania, which involves a satisfaction found in hair pulling, or if she had a more psychiatrically benign habit of chewing on her long hair. This patient's initial psychiatric assessments reported a relatively well-adjusted young girl with few current symptoms of psychiatric concern. It has been suggested in the literature that only a minority of patients with trichobezoars have severe psychiatric disorders.[7, 9] Also of question is whether this patient's bezoars consisted of hair ingested over two years ago, or if she was in fact still surreptitiously chewing her hair. No literature was found documenting bezoars in patients with such distant histories of hair ingestion.

It is interesting that this patient had four distinct bezoars distal to the stomach. It has been suggested that such distal bezoars are the result of fragmentation of gastric bezoars. This differs from Rapunzel Syndrome in which the gastric trichobezoar has a long tail that passes through the pyloric sphincter into the small bowel, reaching the ileocecal valve in one continuous mass. The Rapunzel syndrome is rare, with only about 20 cases described worldwide.[10,11,12]

Usually there are no clinical symptoms until the bezoar reaches considerable size. One report details a 2500 gram bezoar.[13] Smaller bezoars have been found incidentally on laparoscopy. Upon clinical presentation, signs and symptoms may include abdominal pain, loss of appetite, weight-loss, vomiting, loose stools, pancreatitis, jaundice, anemia and hypoalbuminemia. Uncommonly, patients may pass hair fragments in vomitus or stool. Complications of bezoars include ulcers, perforation of the bowel, appendicitis, obstruction and intussusception.[14,15] Diagnosis can be established either by barium swallow or by CT scan. Ultrasonography may also be of use. Definitive diagnosis may be made by endoscopy.

Several nonsurgical treatment options have been explored in the literature. Gastrografin is a low-risk initial option. It is

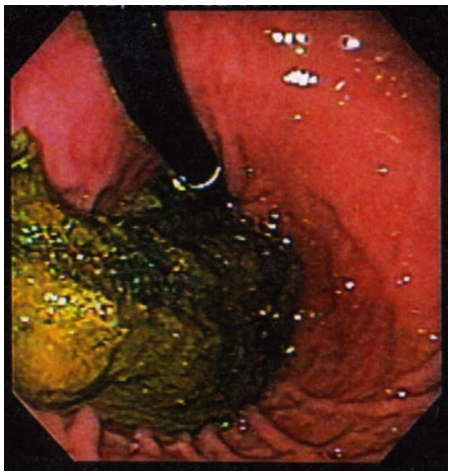

Figure 2. Endoscopy revealed this 11cm x 2.5cm trichobezoar, a green semi-solid collection of hair, in the patient's stomach.

a hyperosmolar water-soluble contrast medium that can be utilized both for its imaging value in evaluating the need for surgery, as well as for a therapeutic role in adhesive small bowel obstruction. Due to its hyperosmolarity, Gastrografin may promote shifting of fluid into the bowel lumen and increase the pressure gradient across an obstructive site. It also decreases bowel wall edema and enhances bowel motility. Gastrografin may dilute bowel content as well, further aiding in the passage of the content through a potentially narrowed lumen.[16]

Endoscopy is an additional non-surgical technique that may offer both diagnostic and therapeutic uses. Gastric bezoars are typically too large at presentation to be removed endoscopically in one piece. However, they may be fragmented with a biopsy device or water jet, and then removed by gastric lavage tube, basket, forceps, or other device.[17] A monopolar diathermy knife with a 15 mm needle called a bezotome has also been utilized in fragmenting large, hardened trichobezoars.[18] This problem has even been addressed by a laser-ignited mini-explosive head used in China.[19] In a study of 100 cases treated by this method, the cure rate was 100 percent. With the exception of one case complicated by gastric perforation, no other complications were observed with this method. As endoscopic removal is usually unsuccessful, the mainstay of treatment remains surgical. Most commonly this entails enterotomy with repair of the resulting bowel defect.[20]

Since recurrence of bezoars of all types is common and may occur in up to 14 percent of patients, prophylaxis of further hair ingestion in patients with trichobezoars is indicated. Treatments may include behavioral therapy combined with anti-depressants, or habit-reversal therapy.[21] In this patient, cutting her hair short enough that she cannot chew it would also be recommended.

In summary, trichobezoars are a rare cause of gastrointestinal distress, predominately affecting school-age and adolescent girls. Physicians evaluating this population for abdominal pain of acute or chronic onset should consider the diagnosis of bezoars in their differential. Once diagnosed, several therapeutic options exist. Selection of treatment should take into account the size, location, and density of the bezoar as well as the degree of obstruction and presence of any comorbid conditions. Once existing bezoars have been successfully removed, attention should be turned to prevention of recurrence.

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ETHICS CASE REPORT

To List or Not To List: Two cases of mentally retarded children in need of solid organ transplants

Steven Lin

Solid organs transplants like kidneys, livers, and hearts are scarce, but they are life-saving. For children with severe mental retardation, the decision whether or not to list them for transplant is a hotly-debated issue. Because many children with severe mental retardation are thought to have a decreased life expectancy, hospitals often use the scarcity argument to deny a child transplant. Should children be denied transplant on the basis of profound mental retardation? This report describes two cases that happened recently at Stanford.

CASE 1: A boy who needs a new liver.

Tony is a ten-year-old boy with Alagille syndrome, an inherited liver disease characterized by a progressive loss of bile ducts within the liver and narrowing of bile ducts outside the liver. The massive buildup of bile has scarred his liver and damaged his heart and lungs due to a narrowing of the pulmonary arteries. He also has complications of severe pruritis, osteoporosis, abnormal growth factors, and numerous problems related to poor nutrition.

As a result of a traumatic accident as a baby, Tony suffered an intracranial hemorrhage that left him profoundly mentally retarded. He is a wheelchair-bound quadriplegic with spastic paralysis. His IQ was not assigned as he was considered "untestable."

The mother is deeply devoted to her child and is willing to do whatever it takes to help him survive. She has been attempting to list him with three different transplant centers, but each has declined because of the severity of his mental retardation. She reports that Tony can recognize family members and ask for objects and actions through eye gaze, gestures, and vocalizations. She also says that he can verbalize the phrase "I love you," and provides a videotape of him at home to the liver team's developmental specialists.

The videotape is viewed by the developmental specialists, who did *not* see any changes in Tony's facial expressions or body movements to suggest recognition of family members. They also did not see any signs of communicative intent, verbalizations of "I love you", or reciprocity with family members. This was confirmed by direct observations of him over a six week period both as an inpatient and outpatient. The developmental specialists viewed the videotape again with the mother, who ultimately agreed with their evaluation.

After receiving the full evaluation, the liver team was inclined not to list Tony for a liver transplant, but nevertheless sought an ethics consultation. However, in discussing the case with the ethics committee, the team noted that, despite his multi-organ system complications, they would likely list Tony if not for his profound mental retardation.

You are part of the ethics committee. You know that it is not uncommon for patients with Alagille syndrome to receive liver transplants. *Should Tony be listed?*

CASE 2: A girl who needs a new kidney.

Cindy is a ten-year-old girl with Wolf-Hirschhorn syndrome, a developmental disorder due to a deletion on chromosome four that has left her with multiple body malformations, recurrent seizures, hypotonia, growth inhibition, and profound mental retardation. In addition, she is suffering from focal glomerulonephritis, which has almost completely destroyed her kidney glomeruli. She is wheelchair-bound with end stage renal disease.

Her parents are deeply devoted to their child and are willing to do whatever it takes to help her survive. They report that Cindy can recognize family members and show a range of emotions through facial expressions, gestures, and vocalizations. They also say that she can indicate dislike by repositioning her body, and can maintain direct eye contact with people in a room through a mirror. She also plays reciprocal games with her family.

The kidney team's developmental specialists are called to evaluate Cindy over a three month period as an inpatient, then for another three months at the dialysis clinic. They confirmed that she can communicate intent through facial expressions, gestures, and vocalizations. They observed that she can play reciprocal games like "peek-a-boo" with her parents, although she needed frequent prompting and became tired after only 20 minutes. These behaviors, which were noted in the initial assessment, became more pronounced and robust over time. By the end of the evaluative period, she could sustain these behaviors for over one hour and acquired a number of new skills, such as recognizing her doctor.

An ethics consult was sought, and you are part of the committee. *Should Cindy be listed?*

DISCUSSION

Cindy was put on the transplant list for a new kidney. Tony was not. It is generally accepted that children with mild to moderate mental retardation should never be categorically

excluded from solid organ transplants. The "gray zone" lies in those who are severely retarded, like the two children presented here. Because of the scarcity of donor organs, hospitals often use mental retardation as a reason *not* to list patients, citing poor long-term outcome and survival as their primary concern.

However, recent studies have shown that this is not true. A prospective, multi-center study in Japan showed that children with mental retardation have excellent kidney transplant outcomes due to consistent support from family members and caregivers. Similar studies of mentally retarded patients receiving renal transplantation in the U.S. have reported one- and three-year survival rates of 100% and 90%, respectively, and excellent compliance with post-transplant medications. However, despite these new studies, listing mentally retarded children for transplant remains a hotly-debated issue.

Often, the presence of reciprocal interaction with family members and loved ones is the "line in the sand" for deciding whether or not to list a mentally retarded child. Many now believe that *all* mentally retarded children deserve to come to the table for rigorous discussion and evaluation, rather than having a few doctors on the transplant team decide their fates.

Thank you to Dr. David Magnus at the Center for Biomedical Ethics for providing the background for these case reports.

Cave of Wonders

Ricky Tong

Medicinal Narratives

Kristen Whitaker

Medicine could not exist without the sharing of personal narrative. The patient interview is based on the notion that the patient, as story-teller, will share his or her experience of health and illness, and that the doctor, as active listener, will be able to take that story and make sense of it in the world of science and medicine. In the act of questioning, we attempt to build a complete picture of the patient, to formulate past and present health state in the context of his or her life into something that we can understand and act upon as healers. At the same time, the practice of story-telling itself can be a powerful healing opportunity and relationship-building moment for both the patient and the doctor. The patient becomes the expert and the doctor is given a glimpse into the window of the actual experience of illness.

As an undergraduate, I was given the opportunity to be a "writing advisor" for a narrative therapy intervention for adolescents with chronic physical illness. The purpose was to develop and implement a pilot, ten-week group psychotherapy intervention for teenagers with chronic physical illnesses ranging from diabetes to cancer to HIV. The group consisted of nine teenage participants, two psychologist facilitators, and two writing advisors: a medical student and myself. We met once a week for ten weeks, for two hours each session. As a writing advisor, my additional role was to meet with half of the teenagers on a weekly basis for individual guidance with their writing. One of the teenagers with whom I worked closely was Ginger, a sixteen-year-old high school student, writer, sister, daughter, friend, and teenager with Type 1 Diabetes Mellitus.

I met Ginger well over a year before I became her writing advisor through a program for teens with chronic health conditions. As I got to know her, I learned that she was the ideal teenager to have diabetes; she had remarkable diabetic control for her age and was mature beyond her years. I was constantly impressed by her dedication to checking her sugars, adjusting her insulin pump, and watching her food intake in such a natural way that sometimes the active management of her body's metabolism went unnoticed. If I wasn't paying close attention and simply absorbed in spending time with her, I would easily miss Ginger counting her carbohydrates and calculating insulin boluses. Soon after I met her, Ginger was also diagnosed with Celiac Disease, an autoimmune intestinal disease characterized by an allergy to gluten, the protein found in specific cereal grains. While some people would be devastated by just a single diagnosis, Ginger faced the second diagnosis with grace and acceptance and adjusted her already restricted diet accordingly. It was almost as if the fact that her body was fighting against itself produced a stronger will inside of her to fight back. By nature, Ginger is not a sympathy-seeker, and she is unquestionably opposed to allowing her illnesses to define her life.

As her writing guide, I came to build a close friendship with Ginger. Through our individual meetings and her deeply personal writings, Ginger shared with me multiple dimensions of her life that I hadn't known in the past. She tackled difficult and often painful topics with complete honesty—her relationships with "healthy" siblings, her belief in God, now challenged by her illness, her uncertainty about the future. She also wrote about many upbeat and refreshingly youthful topics as well—dating, the accepted norms and expectations of high school, the inspiration she drew from other teenagers in the group. Each narrative introduced me to a new aspect of Ginger as she allowed me to see a delicate, vulnerable side of her that I hadn't in the past. One of my favorite narratives that Ginger wrote during our time together was about making the decision to disclose her illnesses to a peer:

> *I was afraid of what he would think. He might think it's contagious or disgusting that I have to prick my fingers all the time. I couldn't help but think about the time when I was checking my blood sugar at school. A guy took one look at the blood on my fingers and said it was gross. I could never go out with someone who thinks that checking my blood sugar is gross…I was also afraid he would think of me as a freak. Not only do I have diabetes, but I have celiac disease too. Most kids, most GIRLS, do not have several diseases like this.*

When I first began working with Ginger, I would have never guessed that she would have shared something like this. The opportunity to write her own narrative became a powerful tool of expression for Ginger. In addition to giving her a chance to share her perspectives on diabetes and celiac disease, it gave her the chance to transform her experience outside of the context of illness, as a teenager dealing with teenage issues. These narratives reminded me that beyond the Ginger I knew—the inspirational model diabetic—there was a teenager dealing with the complexity of life.

Since working with Ginger, I have spent time with other teenagers with chronic illnesses—some, like Ginger, are incredibly adjusted to life with their illness, and some are on the other side of the spectrum. However, regardless of their ability to manage and accept their illness, in listening to their stories I find this remarkable gift of perspective. As Ginger expresses in another one of her writings,

> *Since that day that I gave myself my very first shot, I've learned a lot. Living with a chronic illness is not a life you can truly understand unless you are the one living it. It does different things to different people. It changes you, it changes the way you think and act. Even though everyone with diabetes has pretty much the same guidelines of how they are supposed to take care of themselves, it is really up to the individual on how they deal with it.*

This experienced perspective is especially important for doctors, who may work with patients with chronic illness on a daily basis but have never walked a day in their shoes. It is a perspective that has come out of many narratives that I have read and reflects a need for patients' stories to be heard. We often talk of the incredible power of sympathy for our patients, and we know that we must display empathy and compassion for their struggles. However, it seems equally important to truly listen to their stories, to be completely present in the moments we spend with them, fully acknowledging that the larger lives they lead outside their illness make them the experts about their condition. I have asked Ginger to share one of her own personal narratives for this edition of *H&P* because she is the expert; I was simply fortunate enough to be one of the many people she has inspired along the way. By putting her story into words, I believe that Ginger has created her own meaning of what she has experienced, validated what she has been through, and acknowledged the importance of patient narratives, for both the patient and the physician. As you read her narrative, I hope you are reminded that every patient's story is worth telling.

The Great-Doctor Planet

Ginger Vieira

We call her Ann. When I first met her the day after I was diagnosed with Type 1 Diabetes Mellitus, I was absolutely terrified. I was thirteen years old and, suddenly, these white-coated monsters were telling me I would have to stab my fingers and my body with sharp objects countless times a day for the rest of my life. And obviously, being thirteen, my response was, "Yeah, right!"

And that's when Ann walked in. She taught me the basics of diabetes for about an hour, and then, to my horror, she handed me a syringe and a bottle of insulin.

"Take a look at the lunch they've brought you," she said, pointing to the apple, peanut butter sandwich, carton of milk, and sugar-free pudding on the tray sitting in front of me from the hospital cafeteria.

Slowly, using the carb-counting book she'd given me, I tried to figure out how much insulin I would take for my fifteen-to-one carbohydrate:insulin ratio.

Okay, so… there's fifteen grams of carbohydrates in this apple, thirty grams in the sandwich, fifteen grams in the milk, and twenty grams in the pudding. Okay…I hate math. I think that means I have to take about five and a half units of this insulin. Okay… so… who is going to fill that syringe for me?

"Here," Ann said, handing me the syringe and the insulin.

She wants *me* to do it? Who does this woman think she is?

I told her I couldn't.

"Yes, you can," she said, putting the syringe and insulin in my hands. She told me how to fill the syringe with the same amount of air as the amount of insulin I needed. I pushed the air into the bottle and drew up five and a half units of this liquid that was suddenly becoming one of my new best friends.

"Now," she said, "you're going to pinch the flesh on the back of your arm and slowly push the plunger on the syringe until it's empty."

I looked at her, just to check once more if she was joking, but it was clear by the look on *her* face that she was not.

"You can do it," she said quietly.

And I did.

Ann has never scared me since. She wasn't tough and stern to intimidate me; she was tough and stern to show me that this whole diabetes thing was something I could do.

Over the next eight years, Ann's no-nonsense approach whipped me into shape when I was being lazy about checking my blood sugars as often as I should or treating hypoglycemic cravings with more food than necessary.

But any adult endocrinologist could tell me these things, right? So why is she so special?

When Ann has an appointment with me, she isn't just meeting with one of her clients; she's meeting with *Ginger*. And when she has an appointment with Mike or Fred or Sarah, she's not just meeting with patients or clients; she's meeting with *Mike* and *Fred* and *Sarah*. Ann knows her patients. She knows our hobbies and the sports we like. She knows our parents and how many brothers and sisters we have. And she knows all of these details have an effect on how we take care of our diabetes.

Ann knows our attitudes, our personalities. She knows sometimes Fred forgets to take his insulin after he eats when he's at his friend's house. She knows Mike still has trouble accepting that diabetes is a permanent part of his life and relies on his mother to tell him when to check his blood sugar. And Ann knows Sarah's younger sister tends to get jealous when their mother spends more time driving Sarah to her doctor's appointments than going to her soccer games.

Ann knows I try really hard to count my carbohydrates and check my blood sugar often, but she also knows I'm good at making excuses for it lately while trying to manage my diabetes and also be a busy college student—so, she doesn't let me get away with any nonsense.

Ann knows her patients are different people in different homes with different families and friends and habits. She sees each patient as an individual. She doesn't assume every teenager is lazy and careless. She takes her time and allows herself to get to know her patients.

I've met endocrinologists who walk in the room with three medical students in tow, shake your hand sternly, then order all the students to check your throat for unhealthy thyroids. And while these strangers are practically strangling me, I'm trying to remember what the hell this doctor's name is and what planet he came from, because if he isn't from Ann's planet, I'd prefer he re-launched and went back home.

I've had other doctors and nurse practioners who have talked to me like I was *obviously* some flaky teenybopper who couldn't care less about anything that didn't involve boys and bubblegum. Ann isn't like this.

Eventually, I'll have to find an endocrinologist for adults whom I actually like and trust, because I'm well aware it'll look funny when I'm sitting in the waiting room as a thirty year-old next to six year-olds playing with plastic blocks. Either way, I certainly won't settle for anyone in the medical profession who sees me as just another diabetic in their list of appointments on Monday morning. I'm looking for someone like Ann.

Ginger Veira is currently a junior at Champlain College in Burlington, VT. She writes a weekly diabetes blog for The Health Central Network website.

Ahead of Her Time

Ashley Plant

Mia was ahead of her time from the very moment she arrived. She was born at 36 weeks gestation but grew into a rambunctious infant radiating the adorable smiles only babies can give, those that give you a sudden urge to pinch those round bouncy cheeks. She attained the appropriate percentiles on body mass index charts at the pediatrician's office, hit every developmental milestone, and continued to be a source of absolute joy to her parents and spunky three-year-old brother. Her life was that of a normal baby, with her parents cherishing every moment of innocence and beauty and looking ahead to her having an unhindered future that would doubtless change the world.

Like the unexpected crash of a wave out of rhythm, the four-month mark heralded a great change for Mia and her family—the beginning of Mia's body's rebellion. She began to vomit after breastfeeding, stopped gaining weight, and seemed to reach a wall in development. Anna and Mathai Mammen, Mia's adoring parents, took her to the Gastroenterology clinic at Packard Children's Hospital, where blood tests revealed that Mia was severely anemic and prompted Mia's immediate admittal for treatment and diagnosis.

Tests, procedures, consults, and intensely stressful situations consumed the greater part of the next ten days. Anna and Mathai had expected that watching Mia undergo multiple uncomfortable and painful procedures would be difficult, but their stress was compounded by Mia's "failure to thrive" diagnosis, which required that the hospital staff first rule out parental neglect or ignorance. Despite a warning from Mathai, a physician himself, Anna was unprepared for the attention focused on her, ranging from her breastfeeding technique to the quantity and quality of breastmilk produced.

Mia's dangerously low hematocrit was corrected, but she was discharged without a diagnosis. Although she probably had a metabolic disorder given the constellation of her symptoms, the specific disorder eluded identification. Such began the trial-and-error phase of her care. To improve her weight gain, Mia was discharged with a nasogastric tube and supplemented with formula; however, even the most elemental of formulas caused acute liver failure. Anna and Mathai undertook the task of researching the components of these formulas and made a number of suggestions to the medical teams, but ultimately, Mia could only tolerate Anna's breast milk, but her mother had to follow a very strict diet. Anna once described this diet to me as "dry, boring chicken breasts… and that's it." This solution seemed to work, and Anna embarked on what would end up being two years of breast-feeding and chicken breast-dieting with no diagnosis or respite in sight. They even invested in breast milk from a bank, but that, too, resulted in Mia's suffering. There were many days when Mia would cry for 20 hours straight, sleeping for only one minute at a time. Mia's body was frozen in time with no substantial growth and a slow, progressive loss of important developmental milestones. It doesn't seem to cross our minds that baby steps may not culminate in running and playing for some children like Mia, whose first baby steps were her only ones.

Anna became weak and malnourished herself with two years of breast-feeding on a highly restricted diet. Mentally, she and Mathai had reached their nadir. Mia's brother, Mathew, was also feeling the effects of a family in crisis. Mathew had almost been kicked out of Chinese school for acting out in class, and he once threw a tantrum during one of Mia's many hospitalizations, culminating in his storming out of the room. It is hard for a six-year-old who is as active and intelligent as Mathew to have the patience to deal with his sister's disease. When I had lunch with the Mammens, Mathew jabbered nonstop about soccer, kindergarten, and his new video game and was disappointed when his parents explained to him that I couldn't play because we were talking about Mia. I'm not sure what Mathew must think about this whole situation, but he is as affected by Mia's disease as anyone else.

Mia's health also continued to suffer despite Anna's best efforts at providing nutrition through her breast milk; her hair was turning white and showing other signs of protein deficiency. Breastfeeding was neither sustainable for Anna nor sufficient for Mia, and total parenteral nutrition (TPN), an intravenous food source, represented a shot-in-the-dark hope to keep Mia fed. However, this option was not without its risks. Although Anna's physical health required that she stop breast-feeding, should TPN not work, Anna's milk source would be gone and there would be no alternatives to feeding Mia. Given her mysterious intolerance of elemental formulas, her risk of intolerance was even greater. It came time to think about issues no parent ever wants to think about, let alone set up legal documentation to address. Although Mia's parents have been emotionally taxed with physicians insinuating neglect or gross incompetence on their part, signing a Do Not Resuscitate order for their two-and-half-year-old daughter forced them to confront issues of life that many individuals have never faced. Anna and Mathai had to accept that the physicians were no closer to a diagnosis of this charted "unknown metabolic disease" and that Mia had deteriorated significantly. A recent MRI showed shrinkage and a mysterious deposition of mineral throughout Mia's brain. The image showed a clear deterioration from the first MRI when she was initially admitted. The once vibrant child now appeared with partial vision, mixed tone in her muscles, an enlarged liver, loss of most of her muscle function, and, the worst symptom of all, extreme pain. From a few steps and a crawl, Mia had regressed to being unable to hold her head up again. Anna and Mathai faced these challenges head on, agreeing that the most important goal was to increase her quality of life. With crossed fingers and many prayers, Mia was put on TPN. Thankfully, it was successful. It seemed that if Mia's digestive system could be avoided all together, some of the mutiny inside her could be bypassed.

But after many hospitalizations, bitter realizations of their daughter's dire situation, and placing their lives on hold, Mia's parents took her home and started her palliative care. She was given oxycodone, valium, steroids, and anti-seizure medications and referred to see a gastroenterologist, a neurologist, a developmental biologist, and an endocrinologist regularly. During this lull in the tidal wave of Mia's disease, Anna and her husband finally re-experienced one of the small pleasures of life—going out to dinner, their first opportunity in over two years.

It was during this calm that I went on an appointment with Mia. Anna was surprisingly joyful because she was excited to share with the physician that not only had she gone out to dinner, but she had also eaten what she wanted and had two glasses of wine. Chicken breast dieting and two years of breast-feeding made those two glasses of wine the most appreciated and desired glasses of wine in the world. Yet despite this transient pleasure, there was still the fear of what Mia's future would hold.

This past year, I have had the opportunity to participate in a first-year medical school elective course called Pediatric Chronic Disease, also known as "PALS." The goal of this course is to learn how a chronic disease impacts pediatric patients and their families. Each medical student is paired with a child at Lucile Packard Children's Hospital. I have been extremely fortunate to be paired with two-year-old Mia, and my experiences with her and her family have helped shaped my understanding of the social effects of disease.

I went to the Mammen home to see what daily life with Mia was like. Palliative care was not exactly what I had pictured. Anna slept in a tiny bed with Mia at her side in a room filled with syringes, TPN kits, gauze, and tons of medication. The only vestiges of childhood were Mia's favorite pink plastic horses lining a shelf, one of which her brother had bought her for Christmas, and some frilly dresses Anna had bought her. In the morning, Anna would bathe and dress Mia in a trying fashion. Mia's muscle tone and rigidity forced Anna to get in the shower with Mia and hold her as she attempted to bathe her without Mia slipping out of her hands. Following these baths were the dreaded diaper changes. A regular and unnoticed occurrence for most children, diaper changes for Mia meant whole-body muscle spasms, screams of pain, and sometimes seizures. I apprehensively watched her eke out a tiny smile as Anna dried her from her shower and kissed her cheeks, preparing her for the moment ahead. Then she would place Mia on her back and scramble for the wipes and diaper as Mia's eyes rolled back, her hands flew up by her head, her body began to convulse, and a sound so disturbing it made one stop dead in one's tracks erupted out of the child. As soon as the diaper was on, Anna would hold Mia to her chest, apologizing for her pain and pleading with her to stop. Mia would eventually calm down, her breathing slowing to a normal pace. Mia would then have

her TPN infusion, and Anna would take Mathew to karate and Chinese school—all in a 'normal' day's routine.

To this day, Mia has her good days and her bad days. Some days she will bless her family with her smiles, a small window into Mia's soul, as if she has triumphed for a brief second over the mutiny inside her. She will enjoy stroller rides and listening to children's television with her brother. She even enjoys "playing" Nintendo Wii against Mathew, as Anna slips the controller in Mia's sleeve and wiggles her arm for her. On bad days, pain medication is not even strong enough to take the edge off, and spasms take hold of her body, leaving her in a deep sleep by day's end and exhausting Anna. Bad spurts are further complicated by her erratic sleep schedule. In addition to losing many developmental milestones, she is gradually losing motor control of her extremities. She doesn't make much noise at all anymore except for the repetitive grinding of her teeth, an outlet for her pain. Only an extremely attentive mother can tell when she is in pain and when it is more than normal. Recently, this careful attention has amounted to catching a treatable small bacterial infection around the bottom of Mia's central line that nevertheless required yet another hospitalization. Sadly, Mia's parents have been told that the source of the bacteria was likely

Mia's gut, and that these infections will continue to happen again and again.

Mia today is an infant-sized two-and-a-half-year-old girl with slender extremities, graying hair, and a glazed stare. Despite this sobering image, I can't help standing in awe of her strength as she endures hours of the same vision and physical therapy everyday. I watch as her mother focuses every ounce of her attention on the simple rhythmic movements of her arms and legs and tells her how beautiful and strong she is for persevering. I can't help laughing as her mom tickles her stomach, and Mia's mouth opens as wide as possible, producing a huge grin. After therapy is over, Anna picks up Mia and holds her in her arms, and Mia turns her head up toward her mother, unable to see her but recognizing her touch. They face another day, difficult, but together.

What have I, as a future physician, learned from my experiences with Mia? Perhaps most importantly, as illustrated in some of the anecdotes above, pediatric chronic disease is not easily removed from its context. Mia's entire family has been changed from this experience. Anna once related an experience in the grocery store, where she noticed people starting at her. One woman approached her and asked how old Mia was. Deciding whether or not to lie, she stated that Mia was six months old; however, the nosy bystander was not to be placated and asked her why the baby had so many teeth and so much hair. Annoyed and embarrassed, Anna raced through the check-out line and ran for the door.

Moreover, I have learned that when we do not have answers, it is then that we are particularly called upon to be more than just healers of the body. To this day, Mia does not have a diagnosis and has confused physicians repeatedly, yet each physician has affected the Mammens, having made some days easier than they could have been and some days more trying than necessary. Some physicians have dealt with Anna's hysterics and anger directed towards them over lost blood samples or ignorant staff who have asked whether Mia drinks milk or exclaimed, "Your daughter looks young for her age." Those who sympathized eased Anna's concern and earned her trust knowing someone else also had Mia's best interests at heart. The leadership required to save a child's life pales in comparison to the strength and leadership required of a physician when a child's life cannot be saved.

Lastly, I see from Mia's case precisely how much a patient can affect an individual. Mia may not talk or walk or ask cute questions, but, more than any child I have ever met, Mia has taught me a great deal. She has given me perspective on my own life and my hopes for my career in medicine. Every time I see her I can't help being in awe of her ability to deal with the struggles of living in pain and fighting her disease and still managing to smile as if she were somehow comforting me. I start feeling that somehow this child is ahead of her time, knowing something I don't—possibly some secret hidden meaning of life to which she is guiding me. Meeting Mia, for me, was like a wave to the sand, gone in a moment but leaving an imprint I will never forget. I remember now walking into the PALS Halloween party to meet Mia and Anna for the first time and seeing this smiling bundle dressed up as Yoda. I was hoping I would help Mia in some way by being her PAL, but little did I know that she would do more for me than I could ever do for her.

Escaping the Voices

Jenya Kaufman

My new patient came in overnight and was admitted voluntarily by the on-call resident. With sleep on her mind, the resident handed me the H and P and signed out with a typical one-liner: "Mr. Enton is a 47-year-old man, veteran, with long history of schizoaffective disorder presenting with exacerbation of psychotic symptoms in context of medical non-compliance times 3 weeks. "

Mr. Enton entered the conference room with eyes squinting behind thick glass—he kept his chin up and toward the ceiling. He found his way down into a chair by reaching for the table and sliding his hands across the grey Formica surface until he felt the plastic arms tucked beneath it. Blindly, he pulled the seat away from the table and lowered himself without looking down, the way one might maneuver when the lights are out.

"How are you feeling today?" I asked by rote, a manner I had inadvertently perfected over the last few months.

His head bobbed, he grinned widely exposing two neat rows of milky white teeth, an impressive mouthful for a 47-year-old veteran. He still hadn't raised his eyelids, but his chin was floating downward, and if he chose to use his sight, he would be in a position to see those of us sitting at the table. Mr. Enton giggled like a little girl and finally opened his eyes when they were staring directly at the floor. I waited while he looked at the tiles or his laceless shoes. He mumbled between the nervous laughs, the sounds appearing to escape despite himself. Clearly, he was responding to internal stimuli.

My attending, with her charming Irish accent, asked, "Are you hearing something there, Mr. Enton?"

"The voices..the…th-the voices are telling me to kill myself. Yep, tha-that-that's what they are saying right now." Mr. Enton sneaked a peek around the room before returning his gaze to the floor.

With gentle coaxing and directed questions, he went on to tell us that the phenomenology of his disease had been the same since he was 19 years old in the service. It was during his time in the Navy that he first began to hear the deep base of demon voices whispering in his ears, "It's not worth it…it's time for you to die." The vicious edicts seemed to follow him wherever he went. Mr. Enton enforced this extrapolation with a resigned sigh, "Th-they-they're always with me and al-al-almost always have been."

Mr. Enton emitted an air of hopelessness, yet his voluntary admission to the psychiatric unit suggested some kind of willingness. We explored his past for details about his family. I wanted to help him remember his loved ones, those who might rekindle his will to live. Naïvely, I assumed that a rosy past with the power to heal lay behind this deeply troubled man. "M-mm-mmm-my brother wa-was the only one. He knew me, and when I came out of the service, th-tha-that's when he killed hisself." He cupped his right hand and brought it to his forehead. Long thin fingers stretched down over his glasses, and the heel of his palm rested toward the middle of his mandible. This memory, more than two decades old, could still send a numbing charge through his body. He rocked slowly, back and forth, making the only sound in the room.

"That must have been very hard," cringing just after I uttered this stock comment that sounded flat even before it pierced the quiet.

He laughed heartily and tossed his head back, his eyes now focused on the ceiling's speckled slats. Mr. Enton began muttering something unintelligible between the dwindling chortles. After a few moments his speech returned to a decipherable pattern and, without an effort at eye contact, he mentioned his own attempt at suicide: "O-on-one time I tr-tr-tr-tried too. With a belt, I tr-tr-tried to hang myself wi-with a belt. I didn't want to live af-after my brother died."

Mr. Enton scratched his scraggly beard and waited, seeming to anticipate the next question. Without receiving further empathy, his eyes bolted open, and for the first time during the interview he looked directly toward me: " Ve-ve-very, very tall red demons. I se-see ve-ve-very tall red demons. They're… they.. they are dancing in front of your face right now. They're always laughing at me. Tell, they te-tell me to destroy myself." His eyes snapped shut as fiercely as they had opened. He began rocking in his seat and chuckling in a low rumble. He shook his head slowly from side to side as though he were reading about a local tragedy in the paper.

"I ne-nev-never hurt nobody else, though. No, not anybody. Bu-bu-but sometimes the voices and devils, th-they tell me t-to." He had entered that flow state that people sometimes achieve when they start talking about themselves. It seems to happen quite often when the person has played the role of patient numerous times and has answered all the suggested questions before.

He continued explaining how the voices he hears warn him against others, especially other homeless men. At times, they have encouraged him to kill, stating, "They're after you. Homeless people are bad, you have to do it." Once, the voices became so demanding that he sold his CD player in order to try to buy a gun.

I considered the potential for homicidal behavior from the lanky man sitting before me. His air was gentle and his manner awkward but non-threatening. In fact, in his yellow cotton Veterans' Affairs issue pajamas, he was endearing, and it was hard to imagine a violent thought crossing his mind.

Sometimes the noise in Mr. Enton's head overwhelms him or the dancing devils in front of his eyes won't disappear. It's these times he tends to get on a Greyhound bus. He talks of having traveled all over the country in the last twenty years, unable to feel safe in one place for very long. This nomadic existence is confirmed by his VA record; he has been hospitalized more than thirty times in the past ten years alone. There are remote documents in the system

from Alabama, Connecticut, Arizona, Colorado, Maryland, and California. Each report recounts the above story, the chart reading like a broken record.

I asked Mr. Enton what he thinks has reinforced this persistent pattern, and, after pausing for a moment to consider the question, he explained, "They always fire me. Every job I tried… they always fire me. That's why theys give me di-di-disbility checks." Since the mid-1990s, Mr. Enton has subsisted on Supplemental Security Income, disability pay: $730 per month. "The mo-money c-can p-pay for two, yeah two or three weeks in a motel room and some food, an- an-and beer."

"Beer?" I ask with a rising and unwittingly accusatory tone.

"I will keep drinking alcohol till the day I die. There is nothing else for me to do, I have nothing in my life," he declared with no remorse. According to Mr. Enton he drinks two 40-oz. beers a day, on average. Drinking for Mr. Enton is not rationalized by this despair alone—it has an added benefit for him that bolsters his resistance to sobriety: "Al-alcohol he-helps the voices get quieter."

Risperidone and Mirtazapine are effective psychotropic medications for Mr. Enton, helping to bring the voices down as well. When he has his prescription and takes the medications, he can ignore the commands and reports a side effect profile similar to that of beer: "Sleepy, sometimes my medicines make me very sleepy or… or I feel like I'm drunk… drunk on alcohol." His transient lifestyle, lack of sufficient income, and the disease process itself make it nearly impossible for him to adhere to this regiment and so the vicious cycle continues.

Despite his numerous hospital admissions, he has never stayed in one institution long enough for the institution of a working therapy or to participate in a homeless veterans program and apply for service benefits. After meeting Mr. Enton and reading through his chart, I was moved by his suffering and angered by the missed opportunities to help him. My attending sensed my dismay and suggested I work on rectifying the VA's past mistakes and get him "sorted out."

I was simply determined that Mr. Enton would emerge from this hospital stay with a new and improved life ahead of him. Three days into his stay, having only begun to navigate the bureaucracy of the VA as Mr. Enton's advocate and health care provider, he came into rounds and announced: "I-I-I'm ready for a discharge. The voi-voi-voices are down to a whisper, and I would like to be discharged by tomorrow morning." He stared off at the far corner of the ceiling as he spoke. I was crushed and began rambling about all the good things we were working on lining up for him. He nodded in his usual manner, slowly and in time with his gentle rocking. "I d-don-don't care about mo-money. No, don-don't need it." He smiled and laughed a little. "Are you hearing voices? Are they laughing at you?" I asked, imploring him to give us solid proof that he wasn't ready to go. "Ju-ju-just whispers… nothing clearly. I'd like a discharge, please."

In California, as in most states, strict criteria must be met in order to hold a patient against their will. The LPS Act states that in order to detain a person involuntarily, they must be a danger to themselves, a danger to others, or meet criteria for grave disability. Patients have the right to a hearing and a patient advocate. I have always considered myself to be whole-heartedly in favor of patient autonomy, yet I found myself wishing for a more paternalistic system, one which valued a physician's commitment to beneficence. Mr. Enton had 14 dollars to his name, but he could name three shelters in the area and two soup kitchens. He claimed to have no intentions of hurting himself or anyone else. He presented a clear plan: Use his money to ride the bus to the shelter, which was walking distance from the soup kitchen. He planned to stay there until his next check came through, at which point he planned to buy a bus ticket to Fresno. Clearly, Mr. Enton did not meet LPS criteria for a 14-day hold.

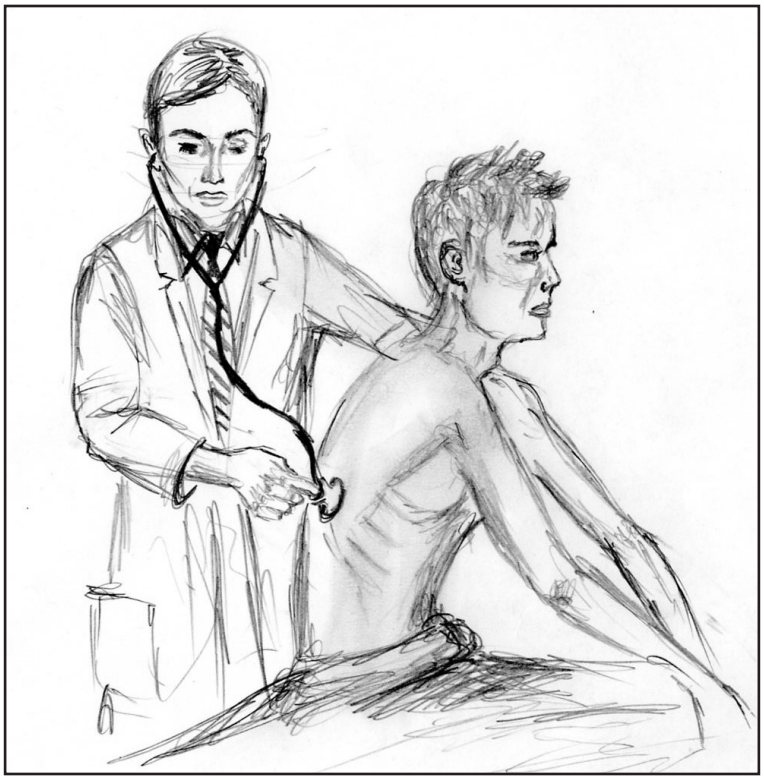
We sent Mr. Enton off with a three-week supply of medication, the address of the San Francisco VA, our best wishes, and instructions to return if he wanted help. This is not an ideal treatment plan, but ultimately it seems preferable to losing a hearing and leaving our patient without any faith in the system. Had we challenged his personal rights, insulting his integrity and autonomy, he might not return if his symptoms again progressed to the point of violence toward himself or others. Mr. Enton has spent close to a quarter-century trying to escape the tortures of his disease process without much success. In the process he has created a life for himself that is manageable more than half the time and is always distinctly his own. But my experience taking care of Mr. Enton leaves me with a nagging question: Can a person's objective quality of life outweigh their subjective experience of life?

Getting Better

Dona Tversky

The nine o'clock sun streamed through fading San Francisco fog and hospital blinds to where Mr. Truwell lay in his bed, having another stroke. Not that anyone of us knew. When Dr. Kaspar examined him late that morning, she bent her long frame over his bed and into his face and stated, "You can barely talk today, can you Mr. Truwell?" Mr. Truwell grunted and blinked in agreement. When his eyes opened again, the left one was wayward, looking out of the window, and the right eye was pleading, a round, warm brown eye, brimming with tears.

Mr. Truwell was 34, an electrician, the father of six-year-old Kayla and four-year-old Ray, Jr. He married Caroline, his high school sweetheart, a year after they started community college, and it was Caroline who first noticed her husband's neurological symptoms last week. "He was stumbling around the room, ran right into the antique lamp, I had to shush him because I was afraid he was going to wake the kids," she explained of the first morning that Mr. Truwell rose, without the sense of balance that allows him to climb poles and repair electrical wires, to swing his son over his head in play, and or just to get out of bed without knocking over lamps. When he turned around to look at his wife, his eyes had lost their usual symmetry; his left pupil drowned, sinking deep into the lower left corner of the space framed by his lids. As if in sympathy, his left arm hung in flaccid paralysis. Mr. Truwell stared at the fallen lamp, wanting to restore it to its vertical position with his dominant left hand but unable to do so. The most he could do to move it was to swing his trunk back and let the arm fly forward.



"I think he is worse today, definitely worse today." Dr. Kaspar stood up straight and looked around the room at her Tuesday morning audience—Maribel, the resident, two students, and the two Truwell women. Mr. Truwell's tall, blond wife in a grapefruit–colored sweat suit had collapsed in a hospital chair by the window, while the older Ms. Truwell in tight jeans and a white t-shirt with "Hot" written across the chest in pink lipstick, stood by her son's bed, holding his hand.

"Worse…," the elder Ms. Truwell repeated, "but that's just *now* right? He's going to the angio suite today and you are going to make him better, right?" I marveled how angio suite rolled off her tongue like "dry cleaners" or "grocery store;" she knew our language.

"Yes, he is going to the angio suite today. In fact, now." Dr. Kaspar looked back at Mr. Truwell: "Yes, right now, can we do that?" She spun around to Maribel, the resident, who gave her a look conveying her sentiments: *You are the attending – whatever you say*.

At two-o'clock that afternoon, Mr. Truwell was wheeled down E3 corridor until it joined with its other arm and then met the central freeway of the hospital, the Main Hall. Impressionist images of boats on water gifted from Silicon Valley donors hung at distant intervals, far enough apart that at attending speed or chasing-attending speed, one could appreciate that there were in fact paintings on the wall, though not their subject matter. If he was awake, Mr. Truwell may have caught a sail or two on his way south, to B3, a sharp left, double doors, a reception area, another set of double doors, a quick right, and then into the room with the whirr.

An hour earlier, a series of doctors had breezed through his hospital room, greeting him, shaking his hand, casually explaining their business while standing above him. "I am Dr. Stein, an anesthesiologist. I will be putting you under today; nothing to worry about; I see you are watching television; no questions I assume, great; I will see you this afternoon." And then the interventional radiologists, and then the neurologists again. The same visitor routine repeated that afternoon; only this time, Mr. Truwell was under a cocktail of anesthesia and there were no introductions, just procedures.

The radiologist injected dye into his vessel, and a team of eight nurses and doctors and technicians watched it diffuse upwards into the left carotid artery where the stream suddenly narrowed to a trickle, like a river dammed by sediment. Beyond the site of blockage, the river expanded

again, and the dye diffused out to fill the vessel.

And then, as easily as the contrast made its way through the artery, a plaque dislodged from a deposit downstream and floated north until it lodged at a fork in the flow and blocked off another branch of the right carotid artery, causing another stroke, the third one this week. It's a complication of the procedure he would be told later—it happens sometimes. And for Mr. Truwell, it meant no more talking and no more moving his left arm.

After the angiography, Mr. Truwell was wheeled back to his room on E3 where Maribel was waiting for him. She performed a quick neurological exam. Maribel's personal distance competes with that of a Delhi native waiting in line for a train. She wanted to ask Mr. Truwell a personal question, so she got up a centimeter from his face, leaned over his bed and tucked in the sheets around his chest. I felt empathetic claustrophobia and instinctively took a step backwards as if to increase the sum total space in the room. "Hi Mr. Truwell!" shouted Maribel too loudly for a man with perfect hearing. "I was hoping that I could videotape you this afternoon, would that be okay? I want to show you at neurology rounds."

Mr. Truwell stared back wide-eyed, motionless. Then his eyes filled with tears and a sob rose from his throat. "Oh, Mr. Truwell, it's okay, we are just doing it to teach the other residents, and it won't take long—I mean, I would just come in alone for ten minutes…"

"And then you will be able to see how far you have come!" The elder Ms. Truwell interrupted Maribel and took over her space, stroking her son's forehead as he shook gently from sobs. Her hand grew wet from the beads of sweat that came along with the tears and she moved to his hair, parting and smoothing it. "You are going to get so much better—they are going to cure you."

Maribel looked at Ms. Truwell with a rare expression of confusion when she heard those words, *getting better*, but she did not interrupt. Ms. Truwell continued, "And then we will look back at the video and laugh, right? We'll laugh!" She peered into her son's glossy marble eyes trapping his head with her two hands to quiet the motion of the sobs. He managed to nod within her grasp. "Okay," he mouthed.

Thomas Tsai

Medicine and the Arts: An Interview with Michael Marmor

Alana Frost

Michael Marmor, M.D., is a Professor of Ophthalmology at Stanford. He is President of the Marmor Foundation and also a part of the multidisciplinary committee which coordinates the "Medicine and the Arts" program. The "Medicine and the Arts" program was recently introduced to first-year medical students through the Practice of Medicine course. Students attended Molière's play The Imaginary Invalid *at San Francisco's Zeum Theater, where actors from the American Conservatory Theater read an adaptation of the script.*

When did you become interested in art?

It's a long history. I was raised in Los Angeles, and my parents collected art. They got to know a number of the modern artists in LA and began to acquire works before they were very well known. I grew up with art in the house—not as something to view on a museum trip, but as a part of routine life.

You recently published a paper on Degas and Monet about their visual problems. Is this an active area of your research?

Yes it is. My academic field is retinal disease and retinal physiology—and how the eye works visually. A corollary of that is studying the visual process and visual dysfunction as relevant to art, and also to music, sports, and other endeavors. I have written two books, *The Eye of the Artist* and *Degas Through his Own Eyes,* which deal with these issues: how functions of vision such as perceiving contrast, color and illusions affect what artists create and what we see in art; and how eye disease and visual loss in different artists have affected their work.

Degas and Monet both had visual failure in their late years, which influenced their painting, but in very different ways. Degas' vision became blurry from retinal disease, so that he could not paint as precisely as before. However, the haziness of his vision smoothed over some of the aberrations in his late works from his point of view, and this may have kept him painting when his pastels began to look crude to others. Monet had dense cataracts which not only blurred his world, but made it brownish so that he could not distinguish colors. It was this loss of color discrimination that was most devastating to his art, because his impressionistic work was based so much on subtle changes of light with the seasons and time of day.

My interest in the interface between medicine and culture, of which vision and art is a portion, is at the core of my efforts to set up this "Medicine and the Arts" program. I have been a part of the Biomedical Ethics and Medical Humanities program at the medical school and have taught undergraduates for many years in the Program in Human Biology. This new initiative was an opportunity to integrate these concepts into the medical curriculum.

Why is having a "Medicine and the Arts" program important in medical education?

Physicians should be more than technicians. Medicine is not solely a matter of applying facts, or conducting research; it is also a means of interacting with individuals and with the health of society at large. Recognizing one's role in society requires education that goes beyond learning biochemistry and syndrome names.

One of the problems of medical school is that it is very demanding. I am certainly not advocating any diminution of physician skills or of the facts that must be learned. However, I think liberal arts should also be a part of medical education. Stanford has been a leader in providing arts events in the medical center, but these voluntary events have variable attendance, since it is often a tough choice for a student to go to a performance when an exam beckons the next day.

The key to what I have envisioned is to have a program of arts events which would be a part of the curriculum, so that participation is expected and required for the whole medical class, and so that the events would be recognized as a part of education. The intent is to have performances or events that are exciting and worthwhile on their own, and concomitantly, to have a program, panel or paper that relates to the event and encourages students to think about what they have seen. Hopefully this will teach about the cultural event for its own sake, and also encourage some reflection about possible implications for the field of medicine.

How are events chosen for the "Medicine and the Arts" program?

The program is coordinated by a committee that consists of Medical School faculty, medical students, and faculty from the Humanities departments on the main campus. We have input from different vantage points to help decide on the events, panels and commentators.

This spring quarter, we will explore two photography exhibits at the Cantor Center for the Arts, which are striking both as art and as social commentary. One is an exhibition of works by Richard Avedon, huge black-and-white photographs of people throughout America. The other exhibit shows works of Gordon Parks, the first black photographer for *Life* magazine. Both photographers show, through their art, the personality and social context of people in this country.

In April the *Lively Arts* at Stanford will host a concert by an extraordinary woman, Dame Evelyn Glennie. She is one of the world's finest percussionists—and is also deaf.

Study of the human figure *Jacqueline Ng*

She has made a preliminary commitment to do a special program with the medical students to talk about her deafness and how it relates to performing as a professional musician. Students will attend both this private session and her public concert. We will also ask faculty from Otolaryngology and the Music Department to add commentary and insight.

It seems that recently in medical education there's been a move to incorporate more of the humanistic aspects of medicine. How do you feel about the "Medicine and the Arts" becoming more of a formalized program, within the context of this shift in medical education?

I have mixed feelings about the formality of arts and ethics education. These programs are important and need to be formalized, given the pressure of so many obligations in medical school. But I think there are some things that cannot be learned from a lecture or tested easily in an exam. Some of the regulatory oversight of teaching in the ethical and cultural sphere, with mandated content, may actually threaten the assimilation of qualities that are better learned by example and experience, and that must be absorbed into the ethos and behavior of students on a very individualistic basis.

I hope these "Medicine and the Arts" events will stand on their own, as exciting music, theater, poetry, art, etc., without our need to tell students why they are good or what they should get out of them. We did not have a test after *The Imaginary Invalid* event, because that was not the point. The goal was to raise sensitivity in an intangible way that will be a little bit different for each person.

I don't expect everyone to enjoy the arts as much or in the same way as I do—we all have things that we like and don't like. But I do hope that all who participate in this program will come away with greater awareness that the arts are an exploration of what we do and of what we value in society. We are a diverse culture in America, and there are many kinds of art; I hope that over time we will look at different forms of expression and all grow as a result.

Translational Medicine: Moliere's Imaginary Invalid

Chantal Forfota

Stanford medical students recently attended a performance of Constance Congdon's adaptation of the Molière play *The Imaginary Invalid* at the American Conservatory Theater (ACT). This was the inaugural event of the "Medicine and the Arts" component of the Practice of Medicine course for first year students.

Wry philosophical satires, Molière's plays lampoon the social institutions of his day, from the Catholic Church to the institution of medicine to the emerging Parisian bourgeoisie. *Le Malade Imaginaire (The Imaginary Invalid),* 1673, Molière's final play, is a satire of the medical profession and a comedic character study of a hypochondriac.

The hypochondriac in question is Monsieur Argan, a wealthy widower. Argan has become increasingly anxious about his health, making him vulnerable to the costly and meretricious ministrations of Dr. Purgon and M. Fleurant, the apothecary, as well as the fussy attentions of his new, financially motivated wife, Beline. Argan is so enthralled by doctors that he has determined to marry off his loyal daughter, Angelique, to Dr. Purgon's dolt of a nephew, Thomas, who has the sole merit of being a physician. The irreverent house servant, Toinette, comes to the rescue by posing as a doctor in disguise and attempting to relieve Argan of his blind acceptance of medical authority.

Thomas Tsai

The doctors in *The Imaginary Invalid* don't represent the profession very well. They are arrogant, ignorant, pompous, self-serving and insincere. Dr. Purgon, as his name implies, is good only for prescribing purgative enemas, and M. Fleurant for composing flowery medical bills that are more poetry than prescription. The doctors play to Argan's hypochondria and encourage his delusion so they may treat him without result and charge him without end. Molière's criticism of medicine is not unfounded. French physicians of the day were well versed in Latin and rhetoric but knew little about anatomy or surgery. Far from being interested in advancing medical science or their own knowledge, they regarded it as sacrilegious to question the ideas of the ancient Greeks. Dr. Purgon praises his nephew Thomas, a recent medical initiate, in the following way:

> *He is attached to the ideas of the ancients with a kind of unquestioning loyalty one only sees in priests, keeping his medical knowledge unsullied by the pretended discoveries of our century concerning the circulation of the blood and other opinions which smack of scientific thought.*

This schema provides a convenient haven for thick-headed ignorance (Thomas), willful deceit (Dr. Purgon), and the atrophy of curiosity in general. Molière makes an explicit connection between medicine and the priesthood, at best a fraternity based on blind faith rather than evidence, and at worst, a corrupt institution more than willing to abuse its power.

Do these less than exemplary doctors hold any relevance for us today? Dr. Purgon uses language as a tool not for communication but for deception and obfuscation:

> *Certainly, he who says parenchyma says both one and the other, because of the great sympathy that exists between them through the means of the vas breve, of the pylorus, and often of the meatus choledici. (81)*

This medical gibberish is a way of disorienting and bewildering Argan, asserting the doctor's authority, and creating a sharp division between those who have been initiated into this language and those who have not. Of course Dr. Purgon's speech is a wild exaggeration, but medical language, like any exclusive jargon, can be used to establish a hierarchy and intimidate those who don't understand it. How often does the impenetrable and coded language of medicine leave patients in the dark?

The play humorously raises issues of compliance and non-compliance as well. Argan unwisely refuses one of M. Fleurant's enemas and receives a barrage of insults instead.

> *I give you up to your bad constitution, to the intemperament of your intestines, to the corruption of your bad blood, to the acrimony of your bile, and to the feculence of your humors!*

Of course we are not meant to curse our patients, even when they are non-compliant. But most doctors have probably succumbed to the temptation at one point or another, because uncooperative patients make an already challenging job harder. No reasonable physician would seriously wish ill upon a patient, but this raises a more subtle issue: that doctors are human and subject to frustration. A grumble under one's breath may not be meant seriously, but it may be taken seriously by the patient. Argan is horrified by the curse—and gives it credence. "They've killed me. I am dead. I am walking around but I'm dead." (89) This may be another shadow of the power of the white coat—its authority may exceed our intentions.

Through the character of Argan, Molière explores the role of imagination in disease. Argan is dyspeptic about the cost of the doctor's bills but he enjoys the artful language and especially the central role that his illness grants him.

> *Doctor Purgon!! What a genius!! Sometimes I*

think he alone understands me in this world…
And then, of course, the main character in the tragedy of my ailments – my bowels…

The ministrations of the doctors are comforting and soothing to Argan. His imagined illness creates a theater in which he plays the lead character at center stage. Is there a "real" ailment at the source of these theatrical symptoms? Is Argan simply seeking a distorted version of love? There is a faint suggestion that Argan may have started to develop these symptoms after the death of his first wife.

Toinette: Your father used to be a smart man and as healthy as a horse.
Angelique: Really? When was that?
Toinette: When your sainted mother was alive.
Angelique: What happened?
Toinette: He started these treatments with Dr. Purgon and Monsieur Fleurant.
Angelique: But wasn't he sick first?
Toinette: Debatable.

If hypochondria is an illness of the imagination, is it due to an excess of imagination, resulting in confabulated symptoms, or a failure of imagination? Perhaps Argan needed a way to avoid his sadness at the loss of his wife and developed concrete symptoms to account for his pains. Although he desperately requires love, Argan is unable to imagine that anyone truly loves him, so he needs proof in the form of constant attention from his doctors, saccharine affection from his new wife, and unquestioning obedience from his daughter and Toinette. Argan's ability to discern, to exercise imaginative judgment, is pathologically askew. He has faith in the wrong people and cannot believe the right ones. Molière suggests that hypochondria is both real and imagined, and demonstrates that the consequences of Argan's hyper- and hypo-active imagination are very real for those around him.

What is the cure for an imaginary illness? Dr. Purgon and M. Fleurant provide Argan with an imaginary cure in the form of infinite ineffectual enemas. Toinette, the house servant, provides Argan with a cure for his imagination. She understands that Argan's condition is psychological and emotional in nature so she helps him restructure his beliefs. Toinette assumes the role of Argan's most esteemed authority figure in the guise of an itinerant physician. First she wins his trust, then she cavalierly suggests that he amputate an arm or pluck out an eye, nudging Argan to shed his absolute faith in the authority of doctors. Toinette goes further in her psychiatric intervention, to conduct several evidence-based experiments. She proves to Argan that his wife's love is false and his daughter's love is true by convincing Argan to pretend to be dead and measuring the quantity and quality of their grief. Toinette thereby relieves Argan of his stunning blindness to the sincerity and insincerity of those nearest to him.

Who or what is really satirized in the play? Argan's self-absorption and slavish need for attention actually make him the most gullible and ridiculous character in the play. There may be a covert parallel to Louis the XIV, notorious for his self-indulgence and famously reliant on others to dress, bathe and rule. Power, in this case, comes from the abililty to manipulate the master. Everyone tries to influence Argan, but in an interesting role reversal, Toinette, the selfless servant, is best able to manage this task. Toinette understands both how to manipulate language and how to see through it. The decadent king and wily playwright are mirrored in the inept master and capable servant. Toinette, like the playwright, does not occupy a highly respected role in seventeenth century French society, but as a skillful manipulator of words, she is able to poke fun at those more powerful than herself and speak the truth with a forked tongue.

The Imaginary Invalid is a tapestry of insincere speech, flattery, prevarication and intentional obfuscation of true motives. At one level this points to what Molière sees as the outright hypocrisy of seventeenth century French bourgeois society, the court of Louis XIV and the Catholic Church. This fabric of falsehoods also raises the question, if Toinette does cure Argan, are her methods honest? In Toinette's approach, the doctor-patient relationship is not one in which orders are issued from master to servant, but one in which the art of communication is as important as prescriptions and prognoses. Toinette uses a skillful combination of honesty and deceit, evidence and belief. She helps Argan to see the truth about his doctors, his wife and his daughter, yet not about himself. She indulges his false beliefs about medicine and stages an elaborately spurious ceremony to induct him into the medical profession himself – to immunize him from the influence of opportunistic quacks. She helps him to become a bit more self-reliant and distinguish those who truly care for him from those who wish to deceive him. Argan is not cured of all of his illusions, but if a desire for genuine love was at the core of his illness, perhaps Argan is on the mend.

Of course, Toinette's methods are problematic. We would not want to consciously manipulate or deceive our patients, even for what we considered to be their own good, but perhaps her approach suggests a subtler point – that the lines between effective communication and conscious manipulation may not always be clear and so the quality of one's intentions must be carefully examined. Maybe good medicine is just such an art – a balancing of experimental evidence with the way it is enacted and realized in the theater of belief.

What is the role of humor in medicine? As Dr. Purgon observes, no one likes a funny doctor at the deathbed, but one of the failings of the doctors in this play is that they take themselves and their art far too seriously. They have lost the ability to question that is at the heart of both critical thinking and humor. Perhaps if we want to teach our doctors to think creatively and critically, we should encourage them to laugh. Laughter, in the right context, can be a genial and disarming way to reach a patient. A shift in perspective can make us smile in the bleakest of circumstances. Perhaps this dual quality of sharpening our critical tools and buoying our ability to find respite, humanity and laughter in difficult moments makes humor one of medicine's finest tools.

Ink

Christina Chao

In steady circles I create ink.
I grind clay against slab,
Diffuse disorder
Through the liquid hill on palette.
The lampblack clings
To water in black spirals
That darken and blur
Like evening behind rooftops.
I study the glossy black mound,
The wide-eyed iris.

Years ago, with the accidental
Tilt of a flat earth,
Ink spilled off stone
And trickled as a viscous vein
Along my leg
Into a crescent morass of carpet,
Remaining long past seasons
Of fallen peaches absorbed
By darkest soil.
Outliving efforts to garden.

Petrified gum on the sidewalk
Borders a coffee shop.
Ink from daily thoughts
Lifts from the newsprint
And presses into my finger pads.
On a napkin I rearrange
Words into dotted lines
Of hazy gray chalk.
When I leave ink has followed
Coins left on the table.

Ricky Tong

Pages soak until water
Is black with words.
I dip a pinky into the pool,
Drip my fluid philosophy
Onto the back of my hand,
Studying its split and sprawl
Through channels of unsmooth skin.
I balance my wrist
To keep the flow from
Deltas between my fingers.

Tip of the brush is stretched
As a horse in full gallop.
Stem translates upright,
I write the word for always.
An exercise in art,
Balancing sun above land
With the curve of an animal's tail.
Meaning is incidental. Permanence
Is the weight of each stroke,
Heavy thought tapers to slender visions.

An Insider's Account: Lessons in Labwork

Steve Minear

Every premed has nightmares about labwork. It scares us still, but most of us do it anyway. I like to tell this story about my first lab job. Pretty much nothing I did was right, and what I did right eventually was proven to be wrong. This should sound a little *too* familiar to all of us. Don't lie. We've all been there.

I sat down at my bench, and planned my experiments for the day. This wasn't too hard, because I did the same exact thing every day. I was busy that summer "optimizing a protocol" for purifying blah-blah something, but it never worked. I knew it didn't work, but my boss knew that it should. So, I was told to repeat it. Again and again. And again. I took my tissue samples out of the freezer. They were surgical sections, and stored in 50ml vials, four to a vial. Whatever rationale was used originally for storing them four to a vial was never passed down, but I soon learned that I did indeed need all four, because two would invariably be frozen together, and a third would fall on the ground, leaving the fourth for me to use.

With my shiny new liver section, my day began. The first step was to "homogenize the tissue." To me, this meant "frappe the meat cutlet into oblivion using the scary and user-unfriendly behemoth blending machine, curiously reminiscent of a horror movie." Assembled in the late Jurassic, all safety switches were broken, necessitating a keen mind to twist all the right levers and nozzles to the proper position. Today's safety error was to not replace the cover screw. Upon pressing the "GO" button, the sample disappeared in a whir of aerosolized fury, flecking my labcoat with liver. Worse, once begun, the homogenizer did not stop until complete, so I had to deal with the loud, open blender for a full minute. It sounded like someone started a chainsaw and threw it down an empty hallway. The lab members across the hall peeked out from behind benches like prairie dogs. With my face redder than my freshly decorated labcoat, I took my sample back to my bench and put in on ice.

The next step was to extract the RNA from the sample. Sounds easy, right? Wrong. The toxic and corrosive extraction buffer was stored in a giant cylinder in the fridge, far too large to simply pour, but with a top too narrow to easily maneuver. Occasionally, I would misjudge the distance from the tub to my waiting tubes. Today was a day of poor judgment, and I instead squirted the buffer onto my arm. Hopping and yelling and dropping everything, I ran to the safety sink. A fellow labmate was walking past, shaking his head. He spoke little English and had never previously or thereafter spoken to me, but he muttered, "Some people were not born to be scientists." I'm not sure if he knew that he was speaking out loud. I suspect he did. After extraction, I put my samples and my forearm on ice.

Later came the exciting part of my day: watching ice melt. I actually sat and watched it melt, because if it melted too much, the experiment was ruined. I typically left this out of my job description at parties and such. Rubbing my sore arm, I watched the ice turn into chunks, floating around and popping lazily. Alone with my thoughts and my ice, I then began to mix up solutions for the coming week.

Whatever lab gods had hexed me that day, they struck next and hardest in the stock room. This room was adjacent to the building's break-room, so all noxious preparations could waft straight out the door, hang a right, and end up on your tuna sandwich. The device used to stir up solutions was conveniently dual-purposed. One knob stirred the solution by spinning a magnet, and the other heated up the plate. Almost as ancient as the Jurassic blender, the etched labels of course had eroded away. I absent-mindedly turned on both the stirrer and heater to full power. Upon dissolution of my solvents, I grabbed the flask, supporting the bottom end. Instantly, my latex glove melted onto the plate, gluing my hand onto a searing hotplate. For the second time that day, I yelped and panicked, dropping the flask onto the ground. My solution, essentially soap, slicked down the whole hallway, running past the break-room in little wet fingers. Reeling backward, my hands went up, taking the glued hotplate with me. The cord came loose and knocked several glass bottles onto the floor on its way over head, following the plate. After several reflexive air-karate chops, the plate tore off, and skidded down the hall, glove flicking behind, waving at me in mockery.

Imagine the perspective of the break room staff. Smash! A giant glass something shatters. Whizzzz… a hotplate with a glove attached slides easily across the field of view. Then, a furious, agitated undergrad with one glove and an icepack, labcoat bloodied, stomps by. You pretend to not notice. He knows that you noticed. How could you not? The only person that *didn't* notice was Frank, the friendly night-janitor, but he would certainly hear about it later from the janitors that helped me clean up my huge mess. I sat at my desk the rest of that day, allowing my unused sample to overmelt and degrade.

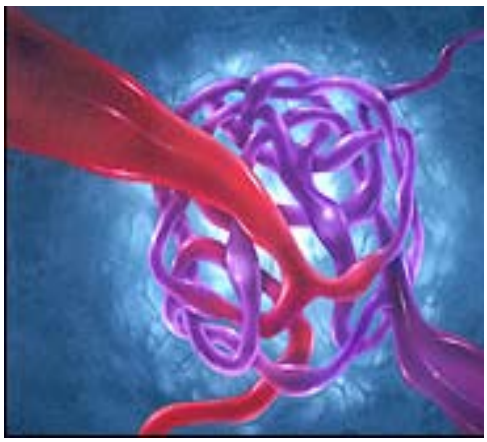
Thus ends my worst lab day ever, second only to "Harvesting Rat Bowel" and "How to Lab Meeting with No Data." I only wanted to go home, curl up in bed, and not be pre-med anymore. My lab days have improved, but I wonder how much of that is inflated because I have been at rock-bottom. Learning to do labwork didn't come easy and came with obstacles. To all the frustrated scientists out there, yearning to accomplish big things, or at least to stop screwing up, take heart. As a wise man, actually Frank the friendly night janitor, once said, "Keep on trucking buddy, you'll get it." And don't worry. We've all been there.

Tangled Webs

Maneesh Singh

"Oh, the tangled webs we weave..." For sufferers of brain arteriovenous malformations (BAVM), this well-known excerpt takes on a grave biological connotation. These congenital abnormalities are best described as snarled tangles of arteries and veins that cause the abnormal shunting of high-pressure arterial blood flow directly into the thin-walled venous system. The central portion of a BAVM, referred to as the *nidus* (from the Latin word for *nest*), is subject to particularly high pressures and vessel wall weakness. This can lead to the development of aneurysms as well as the occurrence of intracranial hemorrhages, noncommunicating hydrocephalus, and catastrophic strokes.

The clinical manifestations of BAVMs are diverse, ranging from symptoms as subtle and insidious as a stiff neck and headache to ones as patent as seizures and sudden loss of consciousness. Surgical removal of the BAVM (craniotomy) is the preferred curative treatment, while focused radiation treatment, known as radiosurgery, has also been successful in the treatment of smaller BAVMs. Unfortunately, it has become clear that pre- and postoperative prognoses of BAVM patients are fraught with uncertainty.



Genes and intracranial bleeds

Upon joining a lab at UCSF, Stanford medical student Achal Achrol began an investigation that would bring some predictability to the clinical course of BAVM patients. Speaking of his early motivations to undertake this research, Achrol says, "It's fascinating to me how little we understand about the diseases of the brain—from the underlying etiologies, to the pathophysiology and natural history, to the reasons for varied responses to therapeutic intervention. That is why what I enjoy most is figuring out one more piece of the puzzle about why cerebrovascular diseases occur…" His early work with a UCSF epidemiological study led to publication of an article in *Stroke* that showed initial presentation with intracranial hemorrhage (ICH)—the most common presenting factor for BAVM patients—to be one of the most important predictors of future ICH. This study concluded that interventions to prevent such hemorrhaging would be of great benefit to patients presenting with ICH, though this advantage would decrease over time.

After finding this clinical predictor of ICH risk in BAVM patients, Achrol and colleagues shifted their focus to single nucleotide polymorphisms (SNPs), minor genetic variations between individuals, in an effort to pinpoint genetic determinants of BAVM development. This study led to a follow-up article in *Stroke* that linked sporadic BAVMs to polymorphisms in genes involved in the hereditary disorder Hereditary Hemorrhagic Telangiectasia (HHT), a familial disorder characterized by numerous, pulmonary AVMs.

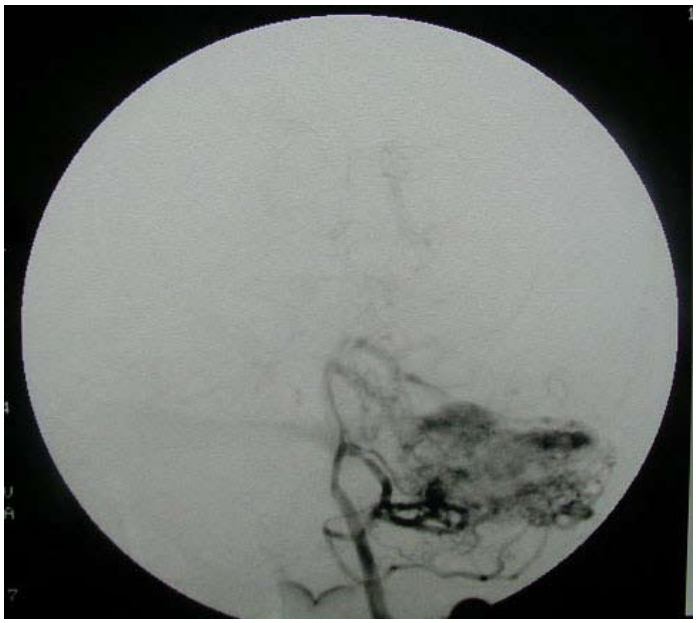
Achrol and colleagues also linked SNPs to hemorrhage risk in BAVM patients. According to Achrol, they looked at many genes but came to focus on those involved in inflammatory response, hypothesizing that "a robust inflammatory response could be linked to the pathogenesis of vessel rupture." Their theory proved accurate and led to the publication of several seminal articles demonstrating an association between genotype of key inflammatory agents (TNF-α and IL-6) and risk of new ICH in the clinical course of BAVMs. "Specifically, we found cases where risk [of ICH] was four times higher if you had [a certain] SNP, and 3.5 times higher if you had another one."

A link to Alzheimer's disease?

One of the SNPs Achrol is speaking of lies within the apolipoprotein E (ApoE) gene, the gene product of which plays a key role in controlling the rate at which protein clumps are deposited into vasculature. Researchers have hypothesized that increased deposition of these clumps, called amyloid, can predispose patients to Alzheimer's disease. Upon observing the connection between ICH and ApoE in his own study, Achrol developed a theory that has led to several current projects: "Amyloid is both a neurodepressant and vasoconstrictor. I believe that amyloid is also recruited by the body as a natural sealant for small vasculature leaks." His theory developed in part from examination of cerebral amyloid angiopathy, a condition in which amyloid is deposited into vasculature at an increased rate. Remarkably, patients with this condition typically present with hemorrhagic stroke due to amyloid deposition.

With this in mind, Achrol and colleagues, in conjunction with Hannes Vogel MD, Associate Chair of Neuropathology, assembled data from post-surgical BAVM patient files and promptly found an association between ApoE SNPs and vascular instability. "We looked at post-surgical files of BAVM patients and found a trend in patients who hemorrhaged—the risk is three times higher in people with a particular ApoE SNP." This link led to Achrol's current investigation of BAVM lesions. Should his theory hold true, he expects to find amyloid present at the site of BAVM ruptures, providing evidence of the body's use of this material as a transient sealant of mini-hemorrhages.

Achrol has begun collecting samples of surgically-excised BAVM lesions and, in a blind study, has preliminary findings showing the presence of amyloid. Further investigation will yield data as to the amount of amyloid present in ruptured vs. intact lesions, potentially establishing a link between degree of amyloid deposition and risk of rupture.



SNPs—A personalized, surgical outcome predictor

Achrol is also collaborating with Steven D. Chang, MD, Associate Professor of Neurosurgery, and Gary K. Steinberg, MD, Chair of the Department of Neurosurgery, to follow postoperative outcomes of BAVM patients treated with a novel tool of radiosurgery, the CyberKnife. Developed by Dr. John Adler, Professor of Neurosurgery, CyberKnife fires several low-dose rays of radiation from different angles that cumulatively produce a high-dosage focal point. In BAVM treatment, the *nidus* is the focus of irradiation while the surrounding brain tissue is left unaffected. Unlike standard invasive surgery, however, the effects of radiosurgery are far from immediate. The procedure requires the targeted cells to undergo mitosis with their irradiated DNA before the lesion can successfully be eliminated. This can take months to years in some patients, and fail to occur at all in others.

With Dr. Chang, Achrol plans to follow patient outcomes and "look at all patient successes, cases where radiosurgery biologically works for them, and compare them to patients [we] call 'radio-resistant patients,' those in which the lesion remains after 2 years." With this study, they hope to use SNPs to select the best candidates for CyberKnife therapy.

When asked what he hopes to achieve from his study of SNPs, Achrol commented that "medicine has long been an observational and population-based science… and this is where the greatest failures arise. Even if a risk is present in a majority of patients or a treatment works for a majority of patients, there is still a significant portion of patients for whom these results do not apply. These are the patients getting unnecessary treatments or having adverse outcomes. What I ultimately hope to achieve is to shed light on some of the genetic and biologic variation that underlie these different outcomes, and eventually make it possible to develop patient-specific treatments that are not based on population trends, but on an understanding of patient-specific biology."

For now Achrol's research seeks to establish a role for SNPs in surgical decision-making, but he sees far more potential for these miniscule variants: "I believe the impact of this type of work will result in better treatment selection, improved treatment outcomes and reduced treatment-related morbidity and mortality, and possibly the development of therapeutic drug interventions where only surgery was an option before."

Genetic Journeys

Amanda Casto

The story of human history is largely about a journey, the sum of many bipedal strides strung out over vast quantities of time. This journey began over 150,000 years ago in East Africa where our species, *Homo sapiens*, first appeared on the fossil record in its anatomically modern form. Natural foragers, these early humans were built to cover long distances, and as their population densities increased, they began to disperse from their homeland. Southern and Western Africa were settled at this time as well as areas of the Sudan and Ethiopian highlands. Of the groups that moved north, one followed the Nile River and its fertile flood plain all the way to its delta on the Mediterranean. The descendents of these travelers—and there may have been as few as fifty of them—reached Europe by 40,000 years ago, Australia by 35,000 years ago, China by 30,000 years ago, and Tierra del Fuego by 12,000 years ago. When recorded history dawned within the last 10,000 years, humanity's dispersal across the face of the globe was nearly complete. The story of this journey did not survive to make it into the pages of our history books. It does, however, survive within humans themselves, encoded in their DNA, and in the past 30 years, researchers have gotten very good at extracting bits of human history from nucleotide sequences.

The differences between human populations on the molecular level were first noticed during World War I. On the battlefields of Europe, blood transfusions became a common part of medical practice and information on the blood types of soldiers from Africa, Europe, and India was collected. Doctors and nurses caring for the wounded began to notice that the frequencies of the ABO blood types varied between soldiers of different backgrounds. These observations were formally analyzed and presented after the war by the Herschfelds, a husband and wife team that had worked in the blood banks on the front. Following this seminal work, a handful of researchers became interested in human molecular variation. They further characterized the geographic distributions of various blood groups, and discovered that many human proteins are polymorphic on the basis of charge. In the mid-1980s, restriction fragment length polymorphism (RFLP) analysis came into being, allowing for the detection of polymorphisms on the genetic level. Alan Wilson and his group at Berkeley were the first to use this technique to investigate human genetic variation on a worldwide scale. They collected DNA from 147 individuals from African, European, Asian, and Oceanic populations. Using multiple restriction enzymes, they discovered a total of 195 sites that were polymorphic in their study group. These sites were used to loosely characterize the relationships between the parent populations of the sampled individuals. Wilson and colleagues chose to use only mitochondrial DNA in their work, primarily because mtDNA follows a simple maternal inheritance pattern that is not complicated by recombination. Keeping with this precedent, the field of human population genetics in its early days focused on mitochondrial DNA markers and the few polymorphic sites found on the Y chromosome. This lasted into the early 1990's when researchers began to look at differences in autosomal markers between populations. Large, allelically complex markers like insertions/deletions and microsatellites were the first to be investigated, followed by single nucleotide polymorphisms. Today, two genomic features are used to characterize human genetic variation: sequence polymorphisms and recombination patterns.

I first began working in human population genetics when, as an undergraduate, I spent a semester at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. There I became involved in a project investigating the origins of the Polynesian Islanders of the South Pacific. Human population geneticists had long been interested in the Polynesians because their population history was originally assumed to be fairly simple—a single founding group colonizing island after island in leapfrog fashion. However, after years of investigation, one important question still remained unanswered—where did this founding population come from? Linguists have linked the Polynesians through their Austronesian languages to the aborigines of Micronesia and Taiwan. They have been at odds with archeologists who believe that Polynesians are an offshoot of the Lapita culture of highland New Guinea. And then there are the geneticists. The work I was involved in at the MPI involved typing hundreds of mtDNA and Y chromosome markers and sequencing a hypervariable region of the mitochrondrial chromosome in samples from nearly 1,000 Polynesian Islanders. The data from this work provided us with no simple answers. The mtDNA of the Islanders was mostly of Micronesian and ultimately mainland Asian origin; their Y chromosome markers, on the other hand, suggested that they descended from New Guinea highlanders. Polynesians were, thus, an admixed population, carrying Micronesian and aboriginal Taiwanese languages, Melanesian cultural traditions, and the genes of both groups with them as they settled the Pacific.

Association studies involve the collection of genomic DNA from both case and control individuals in a given

population and typing these samples for a panel of markers. Markers are typically selected using one of two approaches: the candidate gene approach, where markers that lie in and around particular genes are used; or the genome-wide approach, where selected markers are evenly spaced throughout the genome. Once all selected polymorphisms have been typed, the data are scanned to determine if any marker allele occurs more often in cases than in controls.

Human population genetics and association study work are closely related, because the sample group for an association study is usually composed of people from a single human population. The reason for this is two-fold. First of all, the same disease can have different genetic causes in different populations. One of the most compelling examples of this emerges from hypertension genetic association studies; the genetic variants most strongly associated with having essential hypertension vary between Caucasian, Asian, and African populations. Secondly, the existence of population substructure within a study group can produce false disease-marker associations while masking real associations. Suppose, for instance, an association study is to be done on a study group composed of both Polynesian and Middle Eastern individuals without knowledge of which subjects belong to which population. Because the prevalence of type II diabetes is much lower in the Middle East, most of the case individuals will be Polynesian by chance alone. Thus, this study will make it appear as though any genetic marker that is associated with being Polynesian is also associated with type II diabetes.

Population substructure in association study sample groups is particularly problematic in places like the US that are home to admixed populations. In the US, many of the association studies that are conducted involve white American participants. As a population, Caucasian Americans are far from being a genetically homogenous group; some individuals can be identified with a single ancestral population while others represent complex admixtures of many distinct European and non-European ancestries. Association studies involving white Americans would have much greater power to identify disease-marker associations if the ancestral population or populations of a study participant could be identified. Toward that end, my lab at Stanford is working to identify ancestral informative markers (AIMs) in Europe. AIMs are markers that show significant allelic frequency differences between populations. For instance, if all Irish individuals were AA for a particular marker for which everyone else carried two G alleles, that marker would be an ideal Irish AIM. However, such simple markers do not actually exist, so we rely upon sets of AIMs instead. Our goal is eventually to be able to type a person for our AIM set and, from that data, to be able to determine with reasonable certainty whether he or she is Finnish, Italian, Moroccan, or some combination thereof. It is difficult to estimate at this point just how large such a set of AIMs will be, since European populations are all inter-related in a very complex fashion. Unlike Polynesia, the history of humans in Europe is not one of linear dispersal, but rather one of continuous reversals of movement and fate over a period of 40,000 years.

In Europe, human population genetics becomes particularly personal for me. My genes crossed the Sinai Peninsula 100,000 years ago and then turned northwest, traveling on foot through a series of river valleys into the heart of Europe. Once the travelers that carried them this far grew restless and perhaps somewhat overcrowded in their new home, my genes dispersed along with the proto-Welsh, proto-English, proto-Germans, and likely many others to different corners of the continent. These various genetic lines probably brushed up against each other many times on the stage of European history but were fated to rejoin in my family and myself thousands of miles away across the Atlantic in the mountains of West Virginia. Since then, I have carried my genes to many places, including, two years ago, to Africa. As I landed in Johannesburg one misty morning in June, I could not help but wonder if this was the first time my genes had been back to Africa since they had crossed into the Middle East some one hundred millennia before. In two long days of airplane travel, I had roughly retraced the course of their outward journey: San Francisco to Boston, Boston to London, London to Frankfurt, and then Frankfurt here to Johannesburg. At that point in my musings, standing in the immigration line at the airport, a tourist bureau sign that I had been staring at suddenly cut into my thoughts. I laughed at it as goosebumps ran up my arms. The sign read, "Research show that humans evolved in Africa. Welcome home." I guess I am not the only person who has stood in that line, marveling at the history of her genes.

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