Cases and Reflections
From Mulago

Western Connecticut Health Network
The University of Vermont
Larner College of Medicine
Cases and Reflections
From Mulago
Cases and Reflections from Mulago

Third Edition

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Preface to the Second Edition

The memorandum of understanding signed by Makerere University and Yale University in 2005 led to an innovative approach to the education of students, physicians in training, and faculty members whilst improving the healthcare of patients in Uganda.

The compilation of cases, photographs, and insights represent the dedicated efforts of medical students, house staff, and faculty at the Yale School of Medicine and the Faculty of Medicine at Makerere University. The product of a collaborative effort has blossomed from the opportunity to train in the intense setting of Mulago Hospital: frequently observing clinical syndromes and physical exam findings encountered only in textbooks.

Naturally, the following cases are considered to be primers at best. The discussions within cases were not meant to be authoritative nor were the reflections meant to prepare future physicians in training for all ethical dilemmas. We hope our readers would actively seek out further information and contribute to the educational spirit embraced by the Makerere University Yale University Collaboration (MUYU).

Finally, this text is a work in progress and can only be improved through continuous feedback. We hope our readers will contact us with any suggestions for future editions.

Samit Joshi and Majid Sadigh

Sunrise from Lincoln Flats. Courtesy Esi Nkyekyer
Preface to the Third Edition
Section 1: Cases

Katanga Valley. Courtesy Majid Sadigh.
Schistosomiasis (*S. mansoni*)

Jennifer Edelman and Harriet Mayanja

A 32 year-old fisherman who lives near Lake Victoria presents with several months of abdominal discomfort with increased abdominal girth, occasional dark stool and increased fatigue. The review of symptoms is notable for nonproductive cough for several weeks. He denies any having prior medical problems and does not take any medications. He lives with his brother and drinks alcohol on occasion. His family history is significant for his sister died from AIDS related complications.

On Physical Exam he is Afebrile with: HR 80, BP 105/80, RR 12. General: thin, pleasant, cooperative gentleman appearing as stated age in NAD. HEENT: no scleral icterus, pale conjunctiva, no LAD. Cor: regular S1, S2 without m/r/g. Pulm: CTAB. Abdomen: soft, slightly distended, hepatomegaly with liver edge ~6cm below costal margin, no splenomegaly appreciated, normoactive bowel sounds. Extremities: trace edema, warm with strong distal pulses. Rectal: no gross blood, normal tone, no masses

**What is your differential diagnosis?**

The patient is presenting with a chronic history of gastrointestinal complaints with associated hepatomegaly. The possible causes include a chronic viral hepatitis with potential sequale of cirrhosis or hepatocellular carcinoma. Also possible is gastrointestinal or military tuberculosis, visceral leishmaniasis, or schistosomiasis. Given the patient's occupational exposure, schistosomiasis should be high on one’s differential diagnosis. Schistosomiasis results from an infection with a flatworm: an organism with a cylindrical body, 2 terminal suckers, a digestive tract, and reproductive organs. These trematodes feed on blood and globulins of the human. While there are many species of trematodes, there are several Schistosome species (of varying geographic distribution) carrying major importance involved in human infection: *Schistosoma haematobium*, *Schistosoma mansoni*, and *Schistosoma japonicum*.

**Describe the life cycle of a Schistosome.**

The females (who rest in the males’ gynecophoric channel) produce hundreds of eggs each day that use proteolytic enzymes to migrate to either the bladder (*S. haematobium*) or liver and gastrointestinal tract (*S. mansoni, S. japonicum*). Once the eggs are excreted, ciliated miracidium larva hatch and infect a freshwater snail. Once inside the snail, asexual
reproduction allows them to become sporocytes and eventually cercarial larvae. The cercarial larvae then leave the snail and can survive in fresh water for up to 72 hours. Once a host is found (commonly in warm slow moving water), the cercariae penetrate the skin and migrate to the lungs and liver; inside the liver the cercariae transform into schistosomulae by forming a heptalaminate membrane. Within the portal vein schistosomulae mature and mate; the eggs then migrate to other organ systems, including the bladder or gastrointestinal tract, to begin the cycle again.

*His laboratory values reveal a normal WBC, HCT 35, and PLT 120. Additional studies include normal liver function tests, hepatitis serologies, AFP, and HIV serology.*

**What are the clinical manifestations of Schistosomiasis?**

Patients in endemic areas present after recurrent infection and demonstrate signs and symptoms of chronic infection from high egg burden. The migration of eggs to the bladder, lungs, liver, gastrointestinal tract, and central nervous system result in local inflammation (including granuloma formation) followed by fibrosis. In chronic infections: 1) antibody production and involvement by eosinophils allow for some resistance to re-infection and 2) alterations in the hypersensitivity response result in decreased granuloma formation and intensity of fibrosis.

Migration of *S. haematobium* to the bladder causes inflammation and ulceration clinically manifesting as hematuria; other manifestations include fibrosis, obstructive uropathy, hydronephrosis, and acute kidney injury. Patients may also have a subclinical glomerulonephritis secondary to immune complex deposition disease. Finally, in combination with other carcinogens, bladder squamous cell carcinoma may be seen.

Ova within the pulmonary capillary beds causes end arteritis obliterans and pulmonary hypertension. Genital tract disease (from *S. mansoni*, and *S. haematobium*) may appear as hypertrophic and ulcerative lesions and may facilitate the transmission of HIV and STI's; additionally, manifestations of irregular bleeding, pelvic pain, infertility, and in males- hemospermia may develop. *S. mansoni*, and *S. haematobium* can cause transverse myelitis; *S. japonicum* can cause a meningoencephalitis, focal paralysis, or seizure from granulomatous lesions.
Intestinal involvement from granulomatous inflammation may present with colicky abdominal pain, anorexia, and bloody diarrhea. Lesions ranging from pseudopolyps, ulceration, and bleeding are within the large intestine. Long standing complications include chronic Salmonellosis, contractures of colon, and intussusception.

Within the liver, the eggs of *S. mansoni* and *S. japonicum* cause hepatomegaly and granuloma formation. Fibrosis occurs 5-15 years after initial infection with *S. mansoni*; the time interval is shorter with *S. japonicum*. The classic location is within the periportal spaces leading to Symmers’ pipe stem fibrosis. Sequale from chronic liver disease ensues particularly in those with preexisting cirrhosis or co-infection with Hepatitis C or B.

In contrast to chronic infection, Katayama fever (often seen in returning travelers) is an acute manifestation 2-8 weeks after infection classically seen with *S. japonicum* and *S. mansoni*. The syndrome is a reaction to migrating schistosomulae and is characterized by a pruitic maculopapular eruption in the region of cercarial penetration followed by cough, abdominal pain, fever, fatigue, hepatosplenomegaly, pulmonary infiltrates, and eosinophilia.

**How is the diagnosis of Schistosomiasis made?**

Ultimately, the diagnosis is based upon the patient’s history and clinical features; supportive evidence from examination of stool or urine for schistosome eggs remains the most useful test to perform. The major species can be differentiated by the location of their spine: *S. mansoni* are oval with a lateral spine, *S. haematobium* are oval with a terminal spine, and *S. japonium* are globular without a spine. Anti-Schistosomal antibodies may be used to confirm the diagnosis; however, serology can not differentiate past from active infections and are not available in resource limited settings.

The team seeks to further evaluate for the possibility of schistosomiasis and undertake an examination of the stool as well as an abdominal ultrasound that reveal: oval eggs with lateral spine present and a “bull’s eye” lesion with fibrosis, respectively (see below).
In this patient, the “Bulls Eye” lesion (representing liver fibrosis around the central venous structures) in the presinusoidal region does not alter hepatocyte function and therefore results in normal liver function tests; these findings and the characteristic eggs on stool examination are consistent with Schistosomiasis.

**How do HIV and Schistosomiasis interact?**

Patients with HIV are more susceptible to schistosomiasis and its consequences due to less effective excretion of eggs, impaired granuloma formation, decreased immune response to antigen exposure. On the other hand, schistosomiasis may lead to increased transmission and progression of HIV due to egg deposition induced ulceration and nodularity within the female genital tract.

**How is Schistosomiasis treated?**

The drug of choice is praziquantel. This kills adult worms by affecting membrane permeability through calcium ion channel inhibition within the CNS. The drug kills 65-90% of adult worms but not immature forms or eggs so a repeat course of therapy may be necessary 4-6 weeks after the initial treatment. Mild Side effects (headache, dizziness, abdominal discomfort, fever) are due to dying worms. The use of Praziquantel in neuroschistosomiasis must carefully monitored. Finally, steroids may be used as an adjunct in neuroschistosomiasis and Katayma fever.

**How is Schistosomiasis prevented?**

Avoid contact with contaminated water or wearing protective clothing decrease the risk for transmission. Praziquantel has a half-life of 1 - 1.5 hours and is not effective against eggs or cercarial larvae. Conversely, Artemether has activity against immature schistosomulae as demonstrated in laboratory and clinical trials; the dosing is higher than given for malaria (6 mg/kg) but given every 2 weeks (S. japonicum), 3
weeks (*S. mansoni*), or 4 weeks (*S. haematobium*). Although not demonstrated in mouse models of malaria, theoretically indiscriminant use of Artemether may result in resistant Plasmodial species. (9)

References:

Chronic Hepatitis B

Michael Lee

A 27 year old man presents to Mulago Hospital with complains of increasing abdominal girth. He first started to notice difficulty fitting into his pants about 3 weeks ago. His abdomen began to protrude more and became tense resulting in constant abdominal pain. He denied any constitutional symptoms such as fever or chills, nausea, vomiting, or change in bowel habits. He did note his eyes began to turn yellow a few weeks ago.

He is sexually active with his wife but does not know his HIV status. He also reports long history of alcohol use, up to 10 beers per day for the past 8 years.

On physical exam his vitals are T 98 F, P 90, BP 100/55, RR 22 General: thin looking middle aged man. HEENT: + scleral icterus. no LAD. Lungs: CTAB. Heart: RRR, normal S1/S2, no murmurs. Abdomen: protuberant abdomen, normal active bowel sounds, non-tender, non-distended, + shifting dullness, + fluid wave, an enlarged and nodular liver is palpable, spleen size also mildly enlarged. No caput medusa. Extremities: 1+ pitting pedal edema bilaterally. Neuro: no asterixis

What is your initial differential diagnosis?

Based on history and physical examination the patient is presenting with ascites- that carries a broad differential diagnosis. Cirrhosis is the most common cause of ascites; followed by heart failure, liver cancer, peritoneal carcinomatosis secondary to ovarian cancer, abdominal tuberculosis, nephrotic syndrome, and schistosomiasis. More rare causes include portal or hepatic vein thrombosis, Chlamydia peritonitis, and SLE.

Cirrhosis has multiple etiologies in this region of the world. Most commonly, viral hepatitis (Hepatitis B) and alcohol abuse. Hepatitis B is transmitted percutaneously, sexually, and perinatally affecting 350-400 million individuals internationally- a proportion of which will suffer from cirrhosis and hepatocellular carcinoma (HCC). In areas of high seroprevalence, transmission is likely perinatally. Hepatitis C is more common in northern Uganda and may be transmitted from endemic areas in Sudan.

Additionally, heart failure may cause of ascites and lower extremity edema. Common etiologies for heart failure include hypertension, ischemic heart disease, and previously undiagnosed congenital heart
disease (Tetralogy of Fallot, VSD, patent ductus arteriosus). In Uganda valvular diseases, (particularly rheumatic heart disease) and endomyocardial fibrosis (EMF) are not uncommon causes of heart failure. EMF can result in left and/or right heart failure with resultant exudative, protein rich ascites. Other causes of heart failure include idiopathic dilated cardiomyopathy, viral myocarditis, and restrictive cardiomyopathy.

Finally, infectious etiologies for his ascites include schistosomiasis and abdominal tuberculosis. Schistosomiasis can lead to portal hypertension when the schistosoma eggs get trapped in the portal circulation.

Further workup reveals the following: WBC 8.1, Hg 11, Hct 33.1, Platelets 110. Chemistry: Na 129, K 3.9, Cl 100, HCO3 24, BUN 11, Creat 1.1. ALT 89, AST 76, total bilirubin 3.4. Hepatitis B surface antigen: positive. AFP: pending. Abdominal US: multiple hyperechoic masses within liver; large amounts of ascites.

Does the laboratory data help narrow your differential?

The differential diagnosis for multiple liver lesions includes bacterial abscesses, metastatic cancer to the liver, hydatid (echinococcal) cysts, and amebic liver abscesses. The presence of HBsAg for greater than 6 months defines chronic hepatitis B; the patient’s mild elevation of transaminases also support this diagnosis. Other laboratory data supporting chronic hepatitis B infection include presence of HBV DNA and anti- Hbc. The combination of the patients ascites, masses within the liver, and the presence of a structural nucleocapsid protein- HBsAg allowed the team to narrow the differential diagnosis to HCC due to chronic hepatitis B infection.

Supporting clinical features of the team’s diagnosis are the patient’s signs of decompensated liver disease primarily by jaundice, ascites, and edema. While not present in this case other manifestations include loss of muscle mass, coagulopathy and bleeding, and encephalopathy; vasculitis and arthritis secondary to circulating immune complexes may also occur.

Patients with chronic HBV infection have a lifetime risk of 20-40% for developing HCC. The time period between infection and malignancy is (on average) 30 years; the molecular mechanism by which this occurs is not yet fully understood. Hepatocellular cancer may result from repeated cellular division from the inflammatory response or as result of dysplasia from HBV DNA integration. While HCC tumors have
inactivated HBV genes, viral incorporation at random sites on chromosomes (early in infection) may result in activation of oncogenes or genetic instability from deletions or translocations.

**What factors are important in considering the chronic progression of Hepatitis B infection?**

In highly prevalent areas there are several factors allowing Hepatitis B to progress to a chronic infection. First, HBV covalently closed circular DNA (cccDNA) is incorporated into the host genome which does not allow the body to eradicate the virus. Second, acquisition of Hepatitis B at a young age leads to immunologic tolerance develops as a result of the body being unable to distinguish virus and self. Still a small amount of liver injury occurs in the immunologic tolerance phase- which may be interrupted by reactivations of HBV at any time; this is followed by an attempt at a phase of immune clearance in the later years of life. Finally, persistent active viral replication (measured by HBV DNA) and the absence of HBe-Ag (a soluble nucleocapsid protein which is not transcribed in precore or core promoter HBV mutants) often result in chronic Hepatitis B and progressive liver disease. Unlike HCC, the role of the eight genotypes of Hepatitis B in determining progression of chronic liver disease is not yet known.

For the above mentioned reasons, it is not uncommon to see HCC present at young ages in Uganda. Other important risk factors include patient gender (males are more likely to develop HCC- although this may be confounded by other factors) or co-infection with Hepatitis C, Hepatitis D, or HIV. In this particular patient, the development of HCC in the context of chronic hepatitis B infection was likely hastened by the cofactor carcinogen: alcohol. Unfortunately, informal surveys suggest that Uganda has the highest per capita consumption of alcohol in Africa.

**How would you manage this patient?**

A reasonable approach would be to evaluate the etiology of ascites and further evaluate the liver masses followed by management of the ascites. Diagnostic evaluation would consist of diagnostic and therapeutic paracentesis; in rare occasions, one may send the ascitic fluid for cytology. Serum studies include: Hepatitis B Surface Antigen, Hepatitis C Antibody, Liver function tests include coagulation studies, alpha-feto protein. Ultrasound guided biopsy of the liver mass will confirm the diagnosis.
The mainstay of medical management of ascites is spironolactone and furosemide, which is available in Uganda. Spironolactone can be given at 100 mg daily and furosemide can be given at 40 mg daily.

Ideally, paracentesis, medical management of his ascites, and evaluation of the liver masses would be necessary. However, due to the financial burden, the patient was unable to pursue further work-up of the liver masses. Therefore, for symptom management decreasing the amount of ascites in his abdomen, while temporizing, was achieved through both paracentesis and medical management. A paracentesis was performed but he did not have money to send the fluid for analysis or to evaluate for the concomitant diagnosis of spontaneous bacterial peritonitis (SBP). Without the knowledge of a gram stain or cell count, the medical team decided not to empirically treat him for SBP. The patient’s abdominal pain improved after paracentesis and ultimately he was discharged on spironolactone 100 mg daily without a definitive diagnosis of his liver lesions. Unfortunately, there was no follow-up of this patient. A clinical scenario that is not uncommon.

References:

Abdominal Tuberculosis
Samit Joshi

A.T. is a 42 year-old man with unknown serostatus who is presenting to the Gastroenterology service with an acute on chronic abdominal pain. He has had persistent diffuse abdominal discomfort described as an “aching.” This has been slightly progressive over the past 6 months. He also admits to having diarrhea and malaria [note: malaria is often used to describe fever]. He denies any nausea or vomiting. A family friend believes he has lost a significant amount of weight in the past 4 months. He has not had any sick contacts and has not traveled anywhere recently. He is employed as a market vendor.

On physical examination his vitals are: T 37 °C, BP 100/80, P 115, RR 25. General he is laying in bed and appears uncomfortable. HEENT: no scleral icterus or lymphadenopathy is noted. Cor: RRR with a 2/6 systolic murmur heard equally throughout. Pulm: decreased BS at Right base. Abdomen: BS x 4 (diminished) with a doughy sensation. No hepatomegaly appreciated. Extremities: negative for edema or rash.

What is your differential diagnosis?

A reasonable differential diagnosis of this patient’s non-specific subacute abdominal complaints is led by abdominal tuberculosis and lymphoma. Other entities include: malabsorption from tropical sprue or inflammatory bowel disease, amebiasis, and malignancy from a variety of solid gastrointestinal sources should be considered.

What is Abdominal Tuberculosis?

Abdominal Tuberculosis is the 6th most common extra-pulmonary source of infection and can affect any aspect of the gastrointestinal tract including solid organs, peritoneum, lymph nodes. A higher prevalence of infection exists in patients infected with HIV. The four major mechanisms involved in acquisition are: hematogenous spread from primary lung infection, spread from lymphatics, ingestion of bacilli, or direct spread from other organs. (2) Concomitant pulmonary Tuberculosis is present in less than half of patients. (4)

The presentation may present in either an acute or in a chronic fashion dependent the location within the GI tract and the patient’s immune system (often impacted by HIV infection, age, nutrition, diabetes, alcohol intake). For example, a chronic infection within the small intestine may
present as malnutrition from diarrhea versus an acute small bowel obstruction, perforation, hemorrhage or peritonitis. The most commonly infected site is the ileocecal region: varying from a mass or obstruction to fever and gastrointestinal bleeding. The proposed pathophysiology for increased infection in the ileocecal region is increased stasis, increased lymphoid tissue, and increased absorption. (4) Patients often have nonspecific symptoms of fever, weight loss, abdominal pain, distention, and diarrhea, and anorexia.

The clinician must also consider atypical presentations such as: peptic ulcerative disease, fistulas in the anorectal area, fever of unknown origin, and ascites. (1) The physical exam may mirror the patient’s presentation: tenderness, hepatosplenomegaly, or mass; a “doughy abdomen” is classic but infrequent finding. (4)

His lab values reveal: WBC count is 12, Hgb 9, Platelet 100. His albumin is 3. An ultrasound shows diffuse small bowel lymphadenopathy and thickening of the ileocecal valve.

What are the methodologies employed in the diagnosis of Abdominal Tuberculosis?

In a patient population with high prevalence of HIV, distinguishing between lymphoma and reactive lymphadenopathy from tuberculosis is difficult. The challenging diagnosis rests in a combination of the patient’s clinical picture, radiographic studies, and microbiological evidence. Where available, molecular techniques (ie. PCR) have proven useful in aiding the diagnosis.

Plain abdominal imaging often reveals sequelae of infection: obstruction or perforation. A chest x-ray consistent with Tuberculosis can support the diagnosis although the radiograph may be normal in 50-60% of patients. (3) Finally, ultrasound or CT can suggest the diagnosis if it reveals lymphadenopathy; these tools can also aid in guided biopsy. In a resource limited setting (which shares a disproportionate burden of disease) the use of ultrasound is very important. The ileocecal area often has concentric bowel wall or loop thickening, ulceration, and ascites. (3) Important features of lymphadenopathy range from an increase in number or size of nodes; nodes circular or ovoid in shape from 12-40 mm (mean 20 mm); nodes that range from being well defined to matted; finally lymph nodes may have central hypoechoic areas. (3)

Laboratory values are often nonspecific: leukocytosis (increased neutrophil or lymphocyte predominance), hepatocellular liver injury,
and an elevated ESR. If paracentesis is performed, the fluid is often a cloudy yellow or straw colored and may have an elevated leukocyte count. (4) Additionally a serum to ascites albumin gradient < 1.1 can support the diagnosis; an Adenosine Deaminase (ADA) > 33 U/L has a 97% sensitivity and 100% specificity in a non-cirrhotic patient population (the prevalence of Abdominal Tuberculosis was not reported). (2)

Gross examination through endoscopy or operative laparotomy does not aid in narrowing the diagnosis to Abdominal Tuberculosis. Histology shows caseating granuloma formulation with central necrosis, fibrinolysis, and calcifications. (1) Microbiological evidence of acid-fast bacilli within lymphatic tissue or ascitic fluid is the gold standard (the latter having a lower yield).

The team suspects abdominal tuberculosis.

What are the management options?

Standard four drug therapy (for a goal of 6 months, minimum) can be both therapeutic and diagnostic (if microbiological/histological evidence is unavailable or inconclusive). Surgery is indicated in the management of an acute abdomen or complications of infection such as stricture, obstruction, massive bleed, or perforation. (1,4). The mortality remains high at 5-10%. (1). Several risk factors for higher mortality include: liver disease, HIV, and malignancy.

![Image](image_url)

Ileocecal tuberculosis is demonstrated by uniform and concentric thickening of the wall of terminal ileum. (3)
References:

TB Meningitis (TBM)

Samit Joshi

R.N. is a 42 year old "known ISS" [note ISS = HIV] female presenting with 3 weeks of progressive diffuse headache without radiation. She has been bed-ridden for 3 weeks and has recently been unable to walk. Her family notes she has had 3 days of blurry vision and incomprehensible speech. She has not had a stiff neck. She has decreased oral intake secondary to loss of appetite confirmed by her family members. Her ROS is positive for non-bloody diarrhea, palpitations, and fatigue with associated dizziness; finally she has had 2 days of lower extremity swelling and orthopnea. She has not had any seizure, nausea, vomiting, fever, chills, or constipation.

She is currently followed by the Infectious Diseases Institute Clinic and was diagnosed with HIV in 2006. Her CD4 3 months prior to presentation was 9 at which time she was started on EFV, 3TC, AZT, and Bactrim. She has no allergies and is from the K'LA (sp?) District.

Examination reveals 37º C, BP 100/40, HR 115, RR 26. Pulse oximetry is not available on the ID ward. In General she is a cachectic female older than her stated age in moderate distress. HEENT: NCAT, nuchal rigidity without Brudzinski or Kernig's Sign, MMM, conjunctival pallor, PERRL, Right CN VI lesion, and no cervical/supraclavicular lymphadenopathy. No JVD at 10 degrees. Positive Red Light reflex b/l. Cor: RRR with flow murmur throughout. Chest: Clear b/l. Abdomen: BS x 4, SNT without hepatosplenomegaly, doughy sensation, or peri-umbilical lymphadenopathy. Extremities: pallor throughout with trace LLE. Terry's nails b/l. Neuro: localizes to painful stimuli, inappropriate words, opens eyes spontaneously. Muscle Tone intact throughout but strength 2/5 proximally and distally in the upper and lower extremities.

What is your differential diagnosis?

Given the patient's severe immunosuppressed state a variety of malignant or infectious etiologies may account for her subacute presentation. Malignant causes are led by Progressive Multifocal Leukoencephalopathy or Primary CNS Lymphoma (PCNSL). Although an immunological or virological response to HAART is unknown, her presentation may reflect Immune Reconstitution Inflammatory Syndrome (IRIS) which reflects the rapid recovery of memory CD4 T-cells following the initiation of HAART.
The triad of PML caused by JC Virus is hemianopsia, hemiparesis, and dementia and has a subacute presentation. PCNSL is a NHL (B-cell) propagated by EBV infection that usually presents with seizure, headache, and hemiparesis in the absence of fever.

Leading infectious etiologies include: Fungal, Viral, Mycobacterial, or Parasitic causes. Cryptococcal Meningoencephalitis presents with classic meningial symptoms of headache (for weeks), fever, photophobia, nausea, vomiting, cranial nerve palsies (including blindness) and mental status change.

Cytomegalovirus encephalitis usually presents with 1-2 weeks of fever, mental status change, and headache; rarely, meningismus and radiculopathy in the lower extremities are found. Cerebral Toxoplasmosis is caused by Toxoplasma gondii, an intracellular parasite that causes major focal neurological deficits including seizure, hemiparesis, speech/sensory deficits in the presence of headache and fever.

CNS manifestations of Mycobacterium tuberculosis account for 6% of extrapulmonary tuberculosis and can present with meningitis, tuberculoma (an intracranial mass effect without meningeal symptoms), or tuberculous arachnoiditis (the presence of progressive radiculopathy, parasthesia, and paralysis over weeks-months). Patients with meningitis can present with two weeks of fever, headache, drowsiness, and confusion. Meningial signs are common along with a sixth cranial nerve palsy. Tuberculous meningitis results from either post-primary infection or reactivation and may present along the continuum of three phases: prodromal (malaise, headache, and fever), meningitic (meningismus, headache, cranial nerve palsy), and paralytic (coma, seizure, hemiparesis).

Laboratory Data Reveals: WBC 2 (30% granulocytes, 40% Lymphocytes, 8% Monocytes), HgB 4.7, HCT 15.5, Plt 126. RDW 13.5 and MCV 86. ESR 146. CSF: WBC 300 (predominately lymphocytic), glucose 40, and TP 200.

How does one differentiate the potential etiologies using laboratory or imaging data?

Distinguishing characteristics on neuroimaging for several of the differential diagnoses include:
On the other hand, CT can suggest TB meningitis through: basilar meningeal enhancement, cerebral edema, infarction, or hydrocephalus. In the absence of neuroimaging, the diagnosis is established by a combination of history, physical exam, basic laboratory analysis, and (in some instances) response to treatment. The CSF analysis reveals mononuclear pleocytosis (100-500), CSF protein 100-500, CSF glucose < 45, and positive AFB smear.

**How would you treat TBM?**

Treatment is 4 drug therapy for 2 months followed by 2 drugs (dependent upon resistance testing) for 7-10 months. A 6-8 week taper of dexamethasone does provide a significant mortality benefit, with those who present in the prodromal or meningitic phases. (2) No significant mortality benefit was seen in either those patients presenting with paralytic symptoms or HIV positive individuals (however the mean CD4 was approximately 66 with no patients receiving HAART, see figure C). Reduction in i) brain inflammation/encephalopathy or ii) adverse events (ie. drug induced hepatitis) by use of corticosteroids may explain the mortality benefit. (2)

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<th>PML</th>
<th>Toxoplasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of lesions</td>
<td>Single usually</td>
<td>Multiple usually</td>
<td>Multiple</td>
</tr>
<tr>
<td>Enhancement</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Edema</td>
<td>Yes</td>
<td>None</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Kaplan Meier Curves for patients treated with and without dexamethasone in those who were HIV negative and positive: figure B and C, respectively. (2)
References:

A 22-year-old female is admitted with fever, change in mental status, and two generalized convulsions. She has a prior history of malaria on two different occasions. She is seronegative for HIV 6 months ago.


What is your differential diagnosis?

Given the patient’s acute decompensation and neurological deficits, meningoencephalitis from a bacterial, viral, or parasitic etiology lead the differential diagnosis; hepatic encephalopathy or ruptured cerebral arteriovenous malformation are also possible. Cerebral malaria should be suspected in any patient from with current parasitemia and a depressed mental status. However patients from endemic areas may have asymptomatic parasitemia and therefore alternative explanations (i.e. viral encephalopathy) for their neurological syndrome; therefore, cerebral malaria is a diagnosis of exclusion. (1)

Describe the epidemiology of Malaria:

Malaria is one of the most prevalent human infections worldwide. More than 40% of the world’s population live in malaria-endemic areas yet approximately 60% of malaria related deaths occur in the poorest 20% of the world’s population. Most deaths occur in sub-Saharan Africa with 300 to 500 million cases and 1.5 to 2.7 million deaths annually. Most of these deaths occur in children less than 5 years of age. Only 5 Plasmodia species (of the over 100) are infectious to humans: Plasmodium vivax, P. ovale, P. malariae, P. knowlesi; over 90% of all malaria cases occur in Africa through infection by P. falciparum.

What is Cerebral Malaria?

The WHO defines a case as a patient with coma after seizure, detection of P. falciparum on peripheral blood smear, and exclusion of other causes of encephalopathy or correction of hypoglycemia. The clinical syndrome
should be suspected in patients with detectable parasitemia and any of the following neurologic or systemic characteristics:

Specific neurological deficits by axis include (dependent on the severity of infection):

1. Mental status: depressed mental status, seizure (more common in children), or coma. The latter is an important prognostic factor and may persist up to 72 hours.
2. Cranial Nerves: Sixth cranial nerve palsy due to increased intracranial pressure, absent corneal reflex, disconjugate gaze, increased jaw-jerk reflex, and clenched teeth.
3. Brainstem: abnormal respiratory pattern, decerebrate or decorticate posturing, and in children additional brainstem reflexes may be abnormal (i.e. pupillary).
4. Motor/Reflexes: In adults, symmetric upper motor neuron lesions are found: increased deep tendon reflexes, increased muscle tone, ankle clonus and extensor plantar responses; children more commonly have hypotonia.

Systemic symptoms occur over several days in adults (2): acute kidney injury (most commonly acute tubular necrosis) and metabolic acidosis from loss of bicarbonate and generation of lactic acid (a strong clinical predictor of death). (2, 3) In adults, retinal changes (similar to Roth’s spots), hemorrhages, and papilledema are possible. Finally, shock, acute respiratory distress syndrome, hemolytic anemia and decreased red cell production from suppressed erythropoietin and decreased bone marrow production, and abnormal bleeding may be observed. In children symptoms occur over more rapidly over 1-2 days (2) and include hypoglycemia, fever, vomiting, and hyponatremia; conversely AKI and ARDS are rare. (1)

**Briefly describe the pathophysiology of the CNS manifestations of Malaria:**

Several potential mechanisms may account for coma, seizures, and retinopathy. The diffuse encephalopathy may be metabolic in nature and the seizures, arising from the tempoparietal area, may be multifactorial: hypoxia, ischemia, erythrocyte sequestration; this may be due decreased RBC deformability and adherence to endothelial cells through interactions between knob proteins inserted into the red cell membrane by the mature parasite (P. falciprum erythrocyte membrane protein 1, PfEMP-1) and host ligands (CD36, intercellular adhesion molecule ICAM-1, and vascular adhesion molecule VCAM-1). (4) In addition, P.
falciprum has been known to cause RBC’s to form rosettes: non parasitized RBC’s surround and adhere to a parasitized RBC thereby blocking the flow of blood within the endothelium. Direct effects of parasite toxins (i.e. GPI) and indirect effects through reactive oxygen products with cytokine production (Tumor Necrosis Factor alpha, Lymphotoxin alpha, or Interferon gamma) may result in increased permeability of the Blood Brain Barrier. (3, 5-7)

The peripheral blood smear shown on the following page demonstrates 3+ Plasmodium falciparum. A presumptive diagnosis of severe malaria with cerebral malaria is made.

![Intra-erythrocytic early trophozoite forms of P. falciprum.](image)

Courtesy Samit Joshi

What are the Sequelae of Cerebral Malaria?

The mortality rate in adults and children is approximately 20-50% and primarily results from cardiopulmonary arrest, renal failure, or ARDS. (4-5) A few long-term neurologic sequelae of cerebral malaria have been observed (more commonly in children) such as focal epilepsy, memory impairment, and diffuse white matter damage detected by MRI. (2) Some deficits such as ataxia or hemiparesis may improve over time. The causes of sequelae are not clear.

Does this patient fit W.H.O. Criteria for Severe Malaria?

Severe malaria is frequently associated with P. falciprum (1) and in this host based upon: 1) high clinical concern for cerebral malaria, 2) high concern for pulmonary edema, and 3) potential development of shock. Multiorgan failure is more common in adults than children. (1)
How is Cerebral Malaria managed?

While Cerebral Malaria is a diagnosis of exclusion, treatment should be initiated early in a patient from an endemic area with the clinical syndrome described above. If necessary, management should begin with controlling the patient’s airway and cardiopulmonary status with subsequent treatment of any metabolic derangements or seizure activity. Control of seizures can be controlled with benzodiazepines. In addition to anti-malarial therapy (quinine or artemisine derivatives) given intravenously or intramuscularly empirical antibiotics for bacterial meningitis should be considered. Notable side effects of quinine are hypoglycemia and arrhythmia.

Once therapy is initiated, resolution of coma should occur in 2-3 days (2). Once oral medication can be resumed, a seven day total course of therapy can be given. Adjunctive therapies such as corticosteriods, mannitol, and iron chelators have been studied in small prospective studies with heterogeneous populations, yet in pooled analyses have not shown to be of beneficial. (7)

Given what you know to treat malaria and severe malaria, you administer quinine to her. You also check her labs, especially paying attention to her glucose, CBC and renal function. Before this, you take note that she is tiring out from her increased work of breathing. Unfortunately, you are at a clinic 45 kilometers from Mulago Hospital. You try to get another I.V. in her. While doing this, she has another general tonic clonic seizure. She becomes more hypotensive and then becomes asystolic.
References:

Rheumatic Heart Disease

Laura Gravelin

Ruthie, an 18 year old Luganda speaking female, presents with two weeks of increasing shortness of breath and lower extremity edema. She says her breathing feels difficult just talking and is associated with a non-productive cough that started more than a week ago. She now fatigues easily but denies diaphoresis, chills, facial swelling, or change in her urine output. She has no children and is not taking any medications. She is accompanied by her sister. They are no longer in school and help their mother with the other children at home. No one at home is coughing or has difficulty breathing.

Physical exam reveals 36.8 ºC, P 120, BP 100/70, RR 24, an O2 sat is unavailable. General: she is seated and noted to appear uncomfortable, tachypneic. HEENT: She has no JVD. Pulm: diffuse inspiratory crackles, decreased BS at the right base. Cor: regular and is notable for a pan systolic murmur and a diastolic murmur. Abdomen: tender hepatomegaly. Ext: Good peripheral pulses and 2+ pitting edema; no clubbing nor cyanosis. She has no appreciable stigmata of infective endocarditis.

What is your differential diagnosis?

In this otherwise healthy young female presenting with subacute dyspnea the differential diagnosis is broad. Pulmonary causes include infections: bacterial or viral pneumonia, tuberculous or nontuberculous mycobacterial infection. Pulmonary manifestations of strongyloidiasis or schistosomiasis are possible. Non-infectious causes which are lower on the differential include hemorrhage, rib fracture, or pneumothorax. Given the patient’s murmur’s, cardiac causes include: heart failure, endomyocardial fibrosis, or infective endocarditis (IE). An atypical manifestation of pericarditis is possible.

What is your differential diagnosis for the two murmurs? What are stigmata of infective endocarditis?

Pansystolic murmurs include mitral regurgitation, tricuspid regurgitation, or ventriculoseptal defect. Notable diastolic murmurs are early decrescendo aortic regurgitation, mid-late mitral stenosis, or tricuspid stenosis.

Stigma of IE include: Roth spots (retinal hemorrhage with a pale center), tender splenomegaly, clubbing, splinter hemorrhages, Janeway lesions (non-tender hemorrhagic, or pustular lesions, often on the palms or soles
representing septic emboli), or Osler’s nodes (tender subcutaneous in pulp of digits representing immune complex formation).

The laboratory data available includes a normal WBC and differential, normal chem 7, and ESR of 36. A CXR shows mild cardiomegaly and increased interstitial markings. An EKG is shown here:

What does her EKG reveal?

Rate 111, Rhythm sinus tachycardia, Axis normal, Intervals: PR 158, QRS 84, QTC 288 biphasic p V1, biphasic p in many of the leads. Q III, F. There may be some ST segment elevation in V1-3 with strain pattern: depression V5-6, T wave inversion V4-6, Left ventricle hypertrophy by Cornell criteria (ravl+Sv3>20f>28m).

A transthoracic echocardiogram reveals:

- LVID 6.1cm (3.5-5.7)
- LVSD 5.0cm (2.5-4.5)
- RVD 2.9cm (0.9-2.6)
- LAD 4.5cm (1.7-4.0)

Ejection Fraction 32%, Pulmonary HTN at 50 mm Hg. Global LV hypokinesis, Moderate MR, AI, and TR noted. The posterior leaflet of her mitral valve was fixed and bright - almost calcified appearing (Probably her pan systolic murmur was MR/TR and diastolic was AI.)
What is your diagnosis and how do you manage her?

Leading the differential diagnosis is now congestive dilated cardiomyopathy likely due to rheumatic heart disease. The patient’s clinical presentation correlates with severity of MS and decreased valve area (unavailable on our TTE report). In more advanced stages, pulmonary hypertension and eventual cor pulmonale are possible. After excluding precipitants to tachycardia (anemia, hyperthyroidism, pregnancy, and fever), treatment would begin with diuresis and slowing the heart rate with beta or calcium channel blockade. Where available, persistent symptoms in setting of appropriate therapy would likely lead to intervention such as percutaneous balloon mitral valvuloplasty or open mitral commissurotomy.

How do you diagnosis rheumatic fever?

Jones criteria include 2 major or 1 major plus 1 minor in setting of streptococcal infection:

MAJOR: carditis (present in 60% of patients), polyarthritis (present in 75% of patients), Sydenham’s chorea, Erythema marginatum, or subcutaneous nodules (present in <10% of patients).

MINOR: Migratory arthralgias, fever, elevated acute phase reactants, or prolonged PR interval.

While one should not use one symptom alone for diagnosis of recurrence strict adherence to the above may actual result in under diagnosis of the clinical syndrome. The natural history of the disease is divided into an acute episode and chronic phase. The acute episode, caused by Group A streptococcal infection presents with carditis, tachycardia, decreased left ventricle contractility, pericardial friction rubs and murmur. In the chronic phase, stenosis of the cardiac valves occurs with 40% of patients developing mitral stenosis and 25% developing aortic insufficiency or stenosis. Recurrence occurs on the order of 10% in underdeveloped countries.

References:

Endomyocardial Fibrosis

Brian Montague and Harriet Mayanja

MF is a 13 year old male of Rwandese descent who presents for evaluation of worsening dyspnea and cough. The patient reports that he was well until approximately 3 years prior to admission when he developed palpitations and exertional dyspnea that would limit his playing. Despite his symptoms, his family did not seek medical intervention until last year when he started developing progressive painless abdominal distension. He denied any history of sore throat or skin rashes prior to onset of symptoms. He had received some unknown medications from a local hospital with some improvement but his symptoms continued to progress over intervening years. In the 2 months prior to admission, he noted increasing abdominal distention associated with epigastric pain, orthopnea, paroxysmal nocturnal dyspnea and marked effort intolerance. A productive cough developed during this period characterized by blood streaks in the sputum. The patient described some anorexia and weight loss. He denied drenching night sweats and fevers.

On examination, he was afebrile, HR 120, BP 100/60, RR 28. In General, the patient is sick appearing, small for his stated age and has a “poor blanket sign.”

HEENT: There was no JVD. Cor: notable for PMI in the 5th space, mid clavicular line, regular tachycardia with a S3. A 3/6 systolic murmur was noted at the apex with radiation to the axilla. An additional 1/6 diastolic murmur was additionally noted at the apex. Pulm: He is tachypneic with bronchial breathing noted in the right mammary region anteriorly with dullness to percussion at the same site. Abdomen: gross distension, with an everted umbilicus, moving well with respiration. There were no visible collaterals. The Spleen and liver were palpable. Extremities: No significant edema of the lower or upper extremities and no digital clubbing.

What is the differential diagnosis of this condition in Uganda?

The patient’s subacute to chronic constellation of palpitations, progressive body swelling, dyspnea, in combination with a S3 suggest cardiac failure as the underlying etiology. A primary pulmonary disease is unlikely as it would not explain the palpitations nor would it explain a left ventricular S3. Liver disease is also in the differential diagnosis for ascites, however the palpitations and dyspnea preceded the onset of ascites by several months making this less likely.

The differential diagnosis for congestive heart failure in a young person in Uganda is relatively narrow: postpartum and other nonischemic
cardiomyopathies, rheumatic valvular disease, tuberculous pericarditis, and endomyocardial fibrosis (EMF). The differential can be narrowed further by distinguishing between heart failure due to systolic dysfunction and that showing more of a restrictive physiology (e.g. constrictive pericarditis such as is seen in tuberculous disease and endomyocardial fibrosis).

**What is endomyocardial fibrosis?**

Endomyocardial fibrosis is a relatively uncommon disease, which occurs world-wide in the region known as the wet tropics. Tropical endomyocardial fibrosis was first described in Uganda in 1949. The pathologic features are identical to those of cardiac fibrosis associated with hypereosinophilic syndromes, first described in the 1930’s by Loeffler. In contrast, case series of the tropical form of this disease have not consistently demonstrated eosinophilia present at levels commiserate to those observed in hypereosinophilic syndromes. While genetic markers have been associated with an increased risk of myocardial injury in patients with hypereosinophilic syndromes these studies have not been reproduced in patients with tropical EMF.

Research on the tropical form of endomyocardial fibrosis has been limited to Centers in three countries: Uganda, Brazil and India (Kerala). The etiology is not well understood, but it is uniformly associated with lower socioeconomic status; however the relative ubiquity of this factor in many areas of Uganda makes this association of limited value. In animal models including primates, cassava intake and diets low in protein have been shown to cause a similar pattern of myocardial fibrosis. Researchers in Kerala have advocated for cerium as a potential causative agent based on its presence in high levels in endemic regions, its bioconcentration in tuberous plants, the demonstration of high levels in the sera and myocardial tissues of affected patients, and laboratory studies suggesting both toxic effects of cerium and demonstrable stimulation of fibroblast activity by cerium.

Detailed studies of the clinical parameters associated with endomyocardial fibrosis as well as case series for surgical management of this condition have been reported from Brazil. The adequate prognostic data is limited, in surgical series from Brazil 5-year survival has been estimated in the range of 50%-60%. In Uganda, genetic and familial clustering has been noted with the predominance of disease occurring in patients of Rwandese descent. Arrhythmias, including atrial fibrillation and ventricular tachycardia and valvular compromise are
nonspecific but may also be associated with cases of endomyocardial fibrosis.

**What factors from the patient’s history may aid in narrowing your diagnosis?**

In a female patient, an obstetric history is very important with regard to the risk of peripartum cardiomyopathy. A history of rheumatic fever may be helpful however in this setting is rarely available. In any patient in Africa, it is important to assess a history of HIV and/or prior tuberculosis treatment. While not present in this case, fever, sweats, weight loss, and lymph adenopathy may all be suggestive of a tuberculous disease. Though alcohol related cardiomyopathy is possible, this is less common given the local cost of alcohol and the need for high levels of intake over an extended period of time. Intake of cassava has also been associated with EMF both in epidemiologic and experimental settings, however cassava is a staple of the Ugandan diet and therefore this association is of limited clinical utility.

The features in this case most suggestive of EMF are the young age of onset, his Rwandese descent, poverty (given the poor blanket sign), and the discordance between the amount of ascites and the absence of lower extremity edema.

**What features of the physical exam may assist in narrowing the diagnosis?**

In this case, the patient presents with a somewhat mixed picture including signs suggestive of right-sided heart failure (edema and pleural effusion) but without JVD. There is productive cough with blood tinge that may suggest left sided heart failure with significantly increased pulmonary venous pressures however rales are absent. This may suggest compensated chronic left sided heart failure. An exaggerated pulsus paradoxus might have been useful if present for assessing the extent of restrictive physiology. The murmurs described suggest mitral regurgitation with the possibility of coexistent mitral stenosis. Mitral regurgitant murmurs may be seen in patients with severe systolic dysfunction and in patients with valve destruction due to fibrosing conditions such as EMF. Given the high rates of rheumatic disease in the population findings of mitral stenosis may be incidental.
The patient’s resources are limited. What studies might you consider which could most efficiently guide your diagnosis?

A chest x-ray is cheap and will allow quick assessment of both the cardiac silhouette and significant lung pathology suggestive of pulmonary edema. On careful review, it may be possible to assess for relative prominence of individual heart chambers. Paracentesis may be useful to assess for portal hypertension but in resource limited settings calculating the serum to ascites albumin gradient may not be possible due to the lack of obtaining albumin measurements. Therefore, ascitic fluid total protein is used in lieu of albumin. Low protein levels (< 2.5 g/dL) are consistent with a transudative process secondary to elevations in portal pressure. Protein levels between 2.5 and 6 g/dL are indeterminate and suggest either portal hypertension or a less pronounced local inflammatory process. High protein levels (> 6 g/dL) are reflective of an exudative process intrinsic to the peritoneum itself. Markedly elevated protein levels are commonly reported in association with endomyocardial fibrosis.

A CBC is a cheap but non-specific test. The clinical history is not suggestive of an acute infectious etiology. A high level of eosinophils may be consistent with EMF but the sensitivity and specificity are poor. Electrocardiography may suggest an etiology for the palpitations such as atrial fibrillation or other evidence of chamber hypertrophy or conduction delay. A specific diagnosis of EMF cannot be made based on EKG.
Echocardiography is a commonly available test with good specificity and may establish a presumptive diagnosis of EMF based on several features: 1) fibrosis of the ventricles sparing the outflow tracts, 2) right atrial dilatation, 3) pericardial effusion, 4) signs of valvular failure, and 5) atrial thrombi. Though the classical description is based on a predominance of fibrosis of the right ventricle giving the appearance of the “heart of Africa,” in clinical series, fibrosis of both ventricles has been observed with the distribution varying from series to series.

Additional data shows a WBC of 13,600 with no eosinophilia and ESR 15. Ascitic fluid analysis shows 5 g/dl protein, 55 cells (lymphocyte predominant), negative AFB smear. A SAAG was obtained 1.41 g/dL. LFTs were normal except for a slight elevation of GGT at 60.

A CXR shows a “globular heart.” Echocardiography shows dilatation of the right side of the heart, rounding off at the apex, with minimal pericardial effusion and signs of congestion of the liver.

Have we made a diagnosis?

Ultimately a pathologic diagnosis can be made only at autopsy or through the endomyocardial biopsy. Given the expense, the lack of facilities in most endemic regions, and the high pretest probability of disease, biopsies are generally not performed. The diagnosis then rests upon clinical and echocardiographic features:
1. The host: a young person, of Rwandese descent, of lower socioeconomic status.
2. A clinical history: an initial episode of palpitations or cardiac insufficiency followed by progressive swelling and dyspnea over a period of years.
3. Physical exam: marked ascites disproportionate to the level of lower extremity edema combined with other features of structural cardiac disease, S3, and murmur suggestive of mitral insufficiency.
4. Echocardiography suggesting fibrosis of the ventricles with a typical pattern of rounding off of the apex

What can be done to manage this condition?

Similar to this patient, most patients with EMF present at a very late stage of disease when the level fibrosis is very extensive. Medical management at this stage has been relatively unsuccessful. The mainstays of therapy are identical to those used for other etiologies of CHF: volume reduction with loop diuretics, angiotensin blockade with ACE inhibitors, inotropy support with digoxin. In settings with cardiothoracic surgical support, surgical debridement has been performed including valve reconstruction with short-term success noted in case reports. Cases of cardiac transplantation have also been published from centers in Brazil.

Anecdotal reports from Uganda have suggested that if patients can be identified during the initial stages of the disease, before significant fibrosis has occurred, anti-inflammatory treatments such as corticosteroids may be successful in slow or even arresting the course of disease. Because the initial symptoms are non-specific and the disease occurs in areas with limited health facilities, patients rarely present at this early stage.

What are the future directions for the study of this disease?

The development of EMF is clearly a multifactorial process including: genetic susceptibility, acquired predisposing factors (perhaps malnutrition, cassava, or cerium), and possibly an initiating toxic exposure (potentially trigger of eosinophilia).

Elucidation of each of these components, combined with efforts towards early diagnosis to support trials of disease modifying therapies will be critical to reduce the human costs of this disease. A recent study of echocardiographic screening in Mozambique is encouraging yet given the resource constraints in many affected areas it is difficult to envision
continual screening of the at risk populations. (5) Serologic tests or other clinical profiles capable of identifying patients prior to the development of fibrosis detectable on ultrasound would be ideal. Building upon efforts identifying specific treatments and genetic markers with myocardial fibrosis in hypereosinophilic syndromes may be the ideal approach for further research into the tropical form of EMF. In addition, the growing body of literature of other fibrosing disorders (i.e. nephrogenic systemic fibrosis) may shed light on the pathology of this condition and offer new means for early diagnosis or treatment.

References:

Pulmonary Kaposi’s Sarcoma

Danielle Bender

A 26 yo female from Kampala presents with hemoptysis, pleuritic chest pain, and dyspnea on exertion for 3 weeks. She complains of a painful lesion in her mouth causing decreased oral intake and a swollen gland in her neck for 3 months. She also notes night sweats, decreased appetite, and 10 kg weight loss over one month. Her PMH is significant for herpes zoster in 2005, gonorrhea multiple times, and malaria twice in the past 10 years. She has never been tested for HIV. She is married with no children, and sexually active with her husband only. She works as a nursing assistant in a clinic. She drinks 3-4 beers three times per week and does not smoke.

On physical exam, she is afebrile, HR 80, BP 110/70, RR 24, and oxygen saturation 81% on RA. In General, she is breathing comfortably and speaking in full sentences. HEENT: There are raised lesions on her hard palate with purplish discoloration and superficial hemorrhage. There is a right-sided 3cm firm, mobile anterior cervical lymph node. Pulm: bibasilar fine rales, approximately half way up both lungs without wheezes. No dullness to percussion or egophony is appreciated. Cardiovascular, abdominal and neurologic exams are unremarkable.

What is your differential diagnosis?

The patient’s subacute presentation of respiratory complaints and focal lymphadenopathy make a systemic or pulmonary infection most likely. These include tuberculosis and bacterial or viral pneumonia (of various etiologies). However, the differential diagnosis is narrowed by her immune status. While this patient’s HIV status is unknown, there is a high suspicion that she is HIV seropositive for many reasons: including her demographic (young woman in Sub-Saharan Africa), history of sexually transmitted infections and herpes zoster, significant weight loss, and an oral lesion that may be consistent with Kaposi’s sarcoma. If she indeed is HIV positive, pneumonia from Pneumocystis jiroveci (PCP), disseminated Mycobacterium avium Complex (MAC), or disseminated Histoplasmosis are also considerations. The presence of night sweats, significant weight loss and lymphadenopathy also make malignancy a serious consideration on the differential. If she is HIV positive, her presentation may be consistent with a lymphoma or Kaposi’s sarcoma (KS).
Laboratory Data reveals WBC 2.2 (40% neutrophils, 43% lymphs, 15% monos, 1.6% eos) HgB 10, Hct 30, Plt 88. She is ultimately found to be HIV seropositive with a CD4 count of 54. Her CXR is shown.

Does this objective data help to narrow your differential?

It is important to remember that although patients with HIV can have unique diseases, they are also at increased risk for common diseases and pathogens, such as community acquired bacterial pneumonia. Tuberculosis is the most common pulmonary complication of HIV in Africa, and is high on the differential, although the CXR findings are not typical. Cryptococcal pneumonia is rare in the absence of meningoencephalitis and on CXR can show calcific nodules or an interstitial infiltrates. Pneumonia from Cytomegalovirus is possible but usually presents much more acutely with a diffuse symmetric reticulonodular pattern on CXR that is most prominent in the periphery. Histoplasmosis is endemic in Africa with prominent features including striking cutaneous lesions that are absent in this case. Disseminated MAC is a more indolent infection, usually presenting with nonspecific B-symptoms and is less likely to manifest with significant radiographic findings. Non Hodgkins Lymphoma (NHL) remains on the differential, especially in light of the enlarged cervical lymph node, and can affect the lungs as part of disseminated disease.
The CXR findings of bilateral interstitial infiltrates are classic for both PCP and pulmonary KS. PCP is found in HIV patients with CD4 counts less than 200, and there is a high rate of co-infection with *M. tuberculosis*. Kaposi’s Sarcoma is an AIDS defining malignancy that can affect multiple organ systems, most commonly skin, lungs and GI tract. Given the objective data, the most likely diagnoses are PCP, KS, and NHL.

**How would you make the diagnosis?**

Noninvasive tests like serum LDH levels are often elevated in patients with PCP; this test is quite sensitive, but not specific (as an LDH can be elevated in other pleuopulmonary infections). Ultimately invasive procedures would be necessary. The patient has two areas that could be biopsied to make the definitive diagnosis: either the palatal lesion or the anterior cervical lymph node. While PCP can also be diagnosed with GMS staining of the sputum, if negative BAL may be necessary. Furthermore, KS may be diagnosed by bronchoscopy as 50-75% of those with pulmonary KS will have typical endobronchial lesions; in many cases the endoscopic appearance makes a biopsy unnecessary. Biopsy only has a diagnostic yield of 25-60% (because of the scattered submucosal lesions) and in one series has a 30% risk of serious hemorrhage.

*The patient’s lymph node was biopsied, and revealed whorls of spindle shaped cells with leukocytic infiltration and neovascularization with multiple small blood vessels, consistent with Kaposi’s Sarcoma.*

**Describe the pathogenesis of Kaposi’s Sarcoma, including the role of HIV.**

KS is a low-grade vascular tumor that is thought to be associated with Human Herpes Virus 8 infection (HHV-8). Numerous growth factors and cytokines, including fibroblast growth factor, VEGF, IL-1, IL-6 and IL-8 (and others) mediate the spindle cell growth, angiogenesis and edema of KS. Since the frequency of KS is increased in both organ-transplant recipients and patients with AIDS, immunodeficiency itself leads to increased HHV-8 replication and probably accounts for much of the increased frequency of KS in HIV-infected individuals. Also starting HAART can lead to immune reconstitution and spontaneous regression of KS. However, given a higher incidence of KS in patients with AIDS compared to recipients of organ transplant there may be other factors. HIV may play a direct role in tumorigenesis through the production of cytokines. The HIV-1 transcriptional transactivator (Tat) protein has been shown to induce expression of cytokines and growth of spindle
cells when incubated with KS cells in-vitro. It also activates VEGF receptor on endothelial cells, which may promote vascular proliferation. Therefore, HHV-8 and HIV infection act synergistically to produce KS lesions. The constant reactivation and reinfection by HHV-8 in the setting of immunosuppression appears to be necessary for sustaining the KS lesion.

**Discuss the clinical features of pulmonary Kaposi’s Sarcoma.**

One third of patients with KS have clinically evident pulmonary involvement with symptoms of dyspnea and cough. KS can involve any part of the respiratory system, including the oral cavity, larynx, trachea, lung parenchyma, bronchi, pleura or intrathoracic lymph nodes. Pulmonary involvement usually occurs after mucocutaneous lesions. The symptoms and severity vary, from asymptomatic findings on CXR to severe alveolar hemorrhage and Acute Respiratory Distress Syndrome, but are often nonspecific and indistinguishable from pneumonia.

**How would you treat this patient?**

The mainstay of therapy is the initiation of HAART. HAART is associated with a decreased proportion of new KS cases, regression in the size of existing lesions and possibly improved survival in patients with KS with or without chemotherapy. A retrospective study analyzed patients with KS before HAART (1990-96) and after HAART (1997-2002). While the mean CD4 count and RNA levels were similar, the risk of dying was significantly decreased post HAART (HR 0.24). Therefore, this patient should be started on HAART as soon as possible.

Other treatment modalities include local therapy with intralesional chemotherapy, alitretinoin gel, radiation, laser therapy, and cryotherapy for one or few cutaneous lesions.

Systemic chemotherapy (liposomal doxorubicin or liposomal daunorubicin) is another option for those with widespread skin involvement (>25 lesions), extensive cutaneous KS unresponsive to local treatment, extensive edema or symptomatic visceral involvement.
References:


Wandegeya Market. Courtesy Danielle Bender
**African Burkitt’s Lymphoma (BL)**

Fred Okuku *(in progress)*

A.C. is a 7 year old seronegative girl (HIV negative) referred from Kumi Hospital (district hospital in eastern Uganda). She presented with an 8 week history of rapid right maxillary swelling associated with halitosis, loose teeth, oral bleeding and drooling of saliva. She had earlier presented to a dentist at a local clinic where tooth extraction was performed on the same side of the jaw.

The mom also reports inability to walk and failure to control stool and urine since a week ago. A.C. has had recurrent fevers, night sweats, low appetite and has lost significant weight over the past 8 weeks. She has however no history of cough or history of contact with adults with chronic cough.

Examination reveals 37.6º C, 90/50, 102, 26. Pulse oximetry was not done. In General she is a cachectic. HEENT: neck supple, Brudzinski and Kerning’s Sign were negative., with severe pallor of the conjunctiva, PERRL, no cervical supraclavicular lymphadenopathy, JVP was normal, fundoscopy was normal. Heart: sounds were normal. Chest: Clear bilaterally. Abdomen: bilateral adnexal firm masses, no hepatosplenomegaly, Extremities: mild LLE.. Neuro: Muscle Tone, bulk, reflexes and power (3/5) reduced in both lower limbs intact in upper limbs.

**List your differential diagnosis?**

- Lymphoma with Mets to the spine
- Disseminated TB - spinal TB (pott’s disease) could cause paraplegia

Labs show: WBC 5.5 (50% granulocytes, 20% Lymphocytes, 1% Monocytes), HgB 6.7, HCT 20.5, Plt 170. RDW 13.5 and MCV 86. ESR 60. CSF: malignant pleocytosis numerous tumor cells. RFT: Crea 1.8, Urea 6.9, K+ 6.2, Na+ 138, Ca2+ 1.8, PO4 2.0. LFTs: ALP 90, AST 35, ALT32, GGT 14, LDH 3100.

**What do the Labs above shown? And what precautions would you take?**

Tumour lysis syndrome (TLS).

Prophylaxis with allopurinol and aggressive hydration for > 2 days prior to treatment. + or – alkalinization of urine with NaHco3 (3 amps NaHCO3 in 1 liter of 5% dextrose) to increase solubility of uric acid and decrease risk of urate nephropathy. Treat hyperkalemia,
hyperphosphatemia and hypocalcaemia accordingly. Heamodialysis may be necessary. (MGH handbook 2nd Ed). The TLS is one reason BL may become an oncological emergency.

*Imaging: USS showed ovarian masses bilaterally. Right maxillary x-ray: showed loss of the lamina Dura, tooth extraction and loose teeth.*

![Images of lamina dura and x-ray showing loss of lamina dura]

**What is the significance of the Lamina dura?**

Lamina dura is cortical bone that lines the tooth socket. The African BL which commonly presents with a jaw tumor almost always leads to loss of the Lamina Dura, this can be detected on the jaw xray as shown below.

Note: Primary hyperparathyroidism, osteomalacia and Rickets lead to loss of the lamina dura.
What are the risk factors for the African BL?

- Plasmodium Falciparum Malaria – Malaria is thought to disrupt immune response against EBV infection (1),
- Human immunodeficiency Virus-most AIDS related BLs in the west are EBV negative,
- Socioeconomic factors,
- Herbal exposure (Euphorbiatirucalli spurge) (2).

How is BL managed in Uganda compared to the US?

Although Cyclophosphamide, oncovir(vincristine) and methotrexate (COM) is still the standard treatment of BL in Uganda, elsewhere the standard of care is HyperCVAD.

How is the African BL staged and how does it vary from the American BL?

Because the African BL presents mainly with a jaw tumor the staging criteria is varies from what is employed elsewhere, it was developed by J.Ziegler and Magrath in the 1970’s at the UCI (3).

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>Stage A</td>
<td>Solitary extra-abdominal site</td>
</tr>
<tr>
<td>Stage B</td>
<td>Multiple extra abdominal sites</td>
</tr>
<tr>
<td>Stage C</td>
<td>Intra-abdominal tumor with or without facial tumor</td>
</tr>
<tr>
<td>Stage D</td>
<td>Intra-abdominal tumor (stage C) with sites of tumor other facial for example CNS or bone marrow</td>
</tr>
<tr>
<td>Stage AR</td>
<td>Resected intra-abdominal tumor (about 90% of tumor resected)</td>
</tr>
</tbody>
</table>

References:

Tuberculous Pericarditis

Robyn Scatena

A previously healthy 17 year-old man presents to Mulago Hospital complaining of 3 months of worsening shortness of breath and fatigue. He reports feeling unwell, and on further questioning confirms progressive dyspnea on exertion, occasional fevers and night sweats, and weight loss. He has no known HIV or TB contacts, and does not know his HIV serostatus.

On Physical Examination, his vital signs are: T 99.0°F, HR 130, BP 65/palp, RR 35, 02 sat 88%. General: He is very ill and weak-appearing, diaphoretic, and languid. Cor: tachycardic but regular, with muffled heart sounds. The JVP is modestly elevated at 8cm. Pulm: lungs are clear. Abdomen: full, dull to percussion, nontender, normal bowel sounds, without shifting dullness. Extremities: lower extremities are warm and without edema. There are enlarged bilateral axillary and anterior cervical lymph nodes. His peripheral pulses are barely palpable. Neuro: He is somewhat sleepy but responding to questions appropriately and oriented to person, place, and time.

What is your differential diagnosis?

The presence of muffled heart sounds, elevated JVP and clear lungs suggests fluid in the pericardium as the etiology for hypotension. The full abdomen in this scenario is likely secondary to passive congestion of the portal system as a result of right heart failure. This young patient with a subacute presentation of symptoms in the absence of any active rheumatologic disorder or sequelae of rheumatic fever suggests an infectious etiology for a pericardial effusion. This is supported further by the patient’s symptomatic hypotension, fevers, and weight loss. Many endemic infections in Uganda may be responsible. Besides an idiopathic etiology, enteroviruses may cause either a myocarditis or pericarditis from hematologic dissemination. Purulent bacterial pericarditis (Streptococcus pneumoniae, staphylococci, and gram negative microbes) may result from hematologic seeding, trauma, or extension of a pleuropulmonary or intracardiac infection. Furthermore, reactive culture negative pericarditis can occur after a resolved Neisseria spp. infection. Fungal etiologies include histoplasmosis (either direct infection or sterile inflammatory response to active infection within regional lymph nodes), Candida spp., Aspergillus spp., or Cryptococcus spp. due to the mechanisms mentioned above for bacterial infections. EBV associated lymphoma or Kaposi’s sarcoma may cause malignant
effusions. Highly prevalent however are tuberculous or nontuberculous mycobacteria (*M. avium-intracellulare*) causing an insidious constellation of chest pain, dyspnea, cough, weight loss, and night sweats.

*The chest X-ray demonstrated clear lungs, an enlarged heart, and a small left pleural effusion.*

**What is tuberculous pericarditis?**

Tuberculous pericarditis is the most common etiology of pericardial effusion in sub-saharan Africa (70% of all patients referred for pericardial drainage) due most commonly to retrograde spread from mediastinal lymph nodes to the pericardium. Less likely causes are military tuberculosis or spread from pulmonary infection. A robust immune system is thought to play a role in the development of tuberculous pericarditis, with many authors predicting an increased incidence as HAART therapy becomes more available; but studies are lacking. The presence of mycobacteria in the pericardium causes a delayed hypersensitivity reaction, with the formation of granulomas and exudates over 4 stages:

1. Abundant mycobacteria trigger fibrin and granuloma formation with an associated polymorphonuclear cell response.
2. A serous to serosanguineous effusion develops slowly with an immune response composed of lymphocytes and monocytes.
3. Increased fibrin deposition along the parietal pericardium and granuloma formation occurs as the effusion is reabsorbed.
4. The overwhelming fibrinous response leads to cholesterol crystal deposition and calcification; ultimately this is associated with constriction. (1)

**What are the clinical characteristics of tuberculous pericarditis? What is the impact of HIV co-infection on a patient’s presentation?**

The presentation is usually consistent with progressive pericardial effusion with or without constrictive pericarditis; rapid accumulation will lead to tamponade physiology. Other features that suggest TB as the etiology for a pericardial effusion include fevers, night sweats, weight loss, dyspnea and lymphadenopathy. The Investigation of the Management of Pericarditis in Africa study prospectively evaluated 185 patients in a multi-center study, 40% of whom had clinical features of HIV infection; based upon serological confirmation clinical determination of HIV status had good positive and negative predictive values. Patients with HIV infection more often presented with dyspnea,
evidence of myopericarditis on EKG, cardiomegaly, hemodynamic instability, or NYHA class IV symptoms compared to patients without clinical HIV infection.

An echocardiogram demonstrates a large pericardial effusion with fibrinous stranding.

How is tuberculous pericarditis diagnosed?

The physical exam of a patient with tuberculous pericarditis is often that of a large pericardial effusion: tachycardia, muffled heart sounds, clear lungs, elevated JVP, and a pulsus paradoxus. Classic physical findings include a third heart sound earlier in diastole and higher in pitch than heard in classic CHF; the pericardial knock—the palpable equivalent of an early third heart sound; and a sudden inspiratory splitting of S2.

Chest radiography demonstrates cardiomegaly (90% of patients), findings of active pulmonary tuberculosis (30% of patients), and pleural effusion (40-60% of patients). (1) On transthoracic echocardiogram, pericardial thickness >5mm, tamponade, and fibrinous strands are significantly associated with tuberculous pericarditis. While the tuberculin skin test and extra-pericardial evidence for tuberculosis may not be evident, the diagnosis of tuberculous pericarditis may be presumptive in endemic areas. For example, only 7% of patients in the IMPI trial had microbiological evidence of tuberculosis infection. (6)

Two South African studies of patients presenting with pericardial effusions developed a clinical algorithm for diagnosing tuberculous pericarditis in resource-poor settings:
Clinical Algorithm:

6 points:
86% sensitive,
85% specific.

<table>
<thead>
<tr>
<th>Points</th>
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<tbody>
<tr>
<td>1</td>
<td>Weight loss</td>
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<tr>
<td>1</td>
<td>Night sweats</td>
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<tr>
<td>2</td>
<td>Fevers</td>
</tr>
<tr>
<td>3</td>
<td>Serum globulin &gt;40g/L</td>
</tr>
<tr>
<td>3</td>
<td>Leukocytes &lt;10,000/dL</td>
</tr>
</tbody>
</table>

Ultimately if invasive measures are necessary, pericardial effusion culture is of greater diagnostic value compared to pericardial histology: AFB smear may be positive in up to 42% of patients and culture 53-75% of patients. (1)

Based on the echo findings, the medical team suspects tuberculous pericarditis.

How is tuberculous pericarditis treated?

Treatment may also provide a diagnostic challenge and is comprised of standard anti-TB regimen plus steroid taper. In a few small trials, the addition of steroids to the anti-TB drugs led to improved clinical parameters at 10 weeks, decreased mortality, and need for pericardectomy at 2 years. A similar study of patients with HIV demonstrated a similar, if slightly more robust, benefit for steroids. These studies’ lack of statistical significance was limited by the small sample size. For cases of constrictive pericarditis, pericardectomy is a life-saving surgery, and should be performed if constrictive physiology persists after 6 weeks of medical therapy. The mortality of untreated tuberculous pericarditis approaches 80% in 2 years. With medical therapy and surgery if needed, the mortality is decreased to near 20%. Unfortunately, constrictive pericarditis develops in 20-50% of patients despite anti-tuberculous chemotherapy.

The boy is started on 4-drug therapy plus steroids, and does better over the next few days.

References:


You are called to see a 34 y/o HIV positive man, originally from Kenya, presenting with progressive weakness and shortness of breath over a period of greater than 6 months. These symptoms have been gradually progressive over the entire interval, however, he reports that they have become much worse. During this time, he has also developed a cough productive of scant white sputum. There is no reported history of hemoptysis. He does report some weight loss over the interval, but is unable to quantify how much. He has been living in Uganda for several years. HIV was diagnosed 1 year prior to visit. He has been in care at a local health center, but is not aware of his CD4 count. At the time of his last visit, he was told that he did not meet criteria for treatment and was advised to return in 3 months for follow-up.

Review of symptoms was notably negative for jaundice, dysphagia, odynophagia, nausea/vomiting, diarrhea, constipation, headache, neck stiffness, or episodes of confusion. No other acute or chronic symptoms were reported. The patient reports no other known medical conditions. His current medications include only trimethoprim/sulfamethoxazole tablets, prescribed through his HIV clinic.

On examination, he was noted to be febrile at 39.3 degrees. There was mild to moderate pallor. He was sick appearing, with diffuse body weakness and moderate wasting. Oropharyngeal candidiasis was noted. There was no jugular venous distention. There was no noted cervical lymphadenopathy. Heart was regular rate and rhythm, s1 s2 without noted murmurs, clicks, rubs or gallops. Decreased air movement was noted with dullness to percussion noted over right lung base. Some fine crepitations noted over superior portions of lung on right. Scant crepitations noted over left lung fields, which were not well localized. Abominal examination showed hepatomegaly with question of some ascites. There was mild tenderness to palpation in the right upper quadrant, abdominal examination was otherwise unremarkable. Extremities were without notable clubbing, cyanosis or edema.
A CBC has been requested and is pending and his admission chest x-ray is as shown below.

What is your initial differential diagnosis and how would you approach the evaluation of this patient?

The patient is presenting with subacute to chronic progressive course of fever, cough and chest pain with significant findings on exam and xray of a unilateral right sided pleural effusion and upper lobe parenchymal infiltrates. There is additionally concern on exam for the presence of anemia, tender hepatomegaly and ascites. The suspicion is highest in this case for an infectious etiology. Given his known HIV diagnosis and moderate wasting, he clinically is presenting with WHO stage IV disease and though his CD4 count is unknown at this time, he should be presumed to be significantly immunocompromised.

Amongst the infectious causes of a unilateral pleural effusion are:

1. Tuberculosis disease with pleural focus
2. Complicated parapneumonic effusion due to bacterial pneumonias
3. Atypical presentation of pulmonary cryptococcosis
4. Atypical presentations of opportunistic fungal infections such as histoplasmosis, coccidiomycosis, paracoccidiomycosis
5. Ruptured amoebic liver abscess

Though many malignancies can present with pleural effusions, two malignancies common in HIV:

6. Primary effusion lymphoma
7. Kapsoi’s sarcoma
Given the protracted time course and the high prevalence of tuberculosis in this setting, tuberculosis disease is the most likely infectious cause of these symptoms. A complicated parapneumonic effusion would be less likely given the protracted course of his symptoms. Cryptococcal lung disease is a consideration as well in an immunocompromised patient, however pleural effusions most typically occur in the context of widely disseminated disease and the asymmetry of the lung of involvement would make that diagnosis less likely (Shirley and Baddley). Focal infiltrates and isolated pleural effusions have been described in the context of opportunistic fungal infections such as histoplasmosis, however these presentations are similarly unusual (Huber et al). A ruptured amoebic liver abscess is also a consideration, particularly in light of a right sided effusion and tender hepatomegaly, however it would not explain the right sided pulmonary parenchymal infiltrates and cavitation (Salles et al). The absence of a preceding history of diarrhea or dysentery makes this diagnosis further less likely.

Other considerations may include malignant effusions, particularly primary effusion lymphoma in light of his history of B-symptoms and Kaposi’s sarcoma (Chen et al). Other malignancies of the pleura and the lung, while they may be associated with pleural effusions are less commonly associated with fever. Pulmonary emboli and infarctions can be associated with fever, however, given the time course in this case this diagnosis is unlikely. Pleural effusions in the context of connective tissue disorders such as rheumatoid arthritis typically occur in patients with advanced joint disease.

Initial evaluation for all patients with suspected tuberculosis disease should include a detailed history with particular emphasis on prior treatments received for his symptoms, history of TB testing, diagnosis, and treatment in the past, as well as the status of his HIV disease. Initial investigations should include sputum samples for AFB as well as CD4 count for patients infected with HIV. For patients with pleural effusions, a diagnostic thoracentesis is indicated to evaluate for possible empyema.

The patient reports no prior evaluation for TB. He has not received any prior antibiotics for these symptoms. CD4 results were not available from his outpatient records. CD4 count performed in the hospital was 37 with a CD4 percentage of four. How does this information impact your differential diagnosis?
Tuberculosis disease remains most likely diagnosis, however the low CD4 count puts him at risk for both more severe presentations of typical infections as well as atypical infections. For patients with bacterial pneumonias and very low CD4 counts, Staph. aureus and Pseudomonas sp. are amongst the most common pathogens. The subacute course of his illness makes infection with either of these organisms less likely.

**What are the key findings on the chest X-ray which have implications for the diagnosis and management of his condition?**

This is an underpenetrated with notable findings of a large right sided pleural effusion, right lower lobe atelectasis. There are also heterogenous opacities in the right upper lobe. There is a lack of mediastinal shift despite the apparently large effusion, likely reflecting the effect of the volume loss due to the loss of lung volume on the right.

The yield of sputum samples in patients with primarily pleural-based tuberculosis disease is limited. Cough, when present, is frequently non productive. Induced sputum samples may yield positive cultures in as many as 50% of patients, however smear positivity rates remain low. The yield of pleural fluid analyses by smear and by culture is low, contributing to a diagnosis in less than 15% of cases. Pleural biopsy has been shown to be most diagnostic with positive cultures in as many as 60% of cases and suggestive histologic patterns in nearly 80% of cases. Positive AFB smears of pleural tissues can be found in 17% of patients. Using histologic as evidence of the diagnosis, pleural biopsies offer the greatest possibility for rapid diagnosis of TB disease of the pleura.

*A diagnostic thoracentesis and pleural biopsy were performed. The total white blood cell count in the pleural fluid was 750 with 90% lymphocytes. Pleural fluid protein was 6.2 g/dL and LDH was 1535 IU/L. Serum protein was 9.3 g/dL and serum LDH was 714 IU/L. AFB smears of the pleural fluid and histologic sections were negative.*

**What is your diagnosis? Would you start treatment?**

The pleural fluid studies are consistent with an exudative effusion by Light’s criteria (Pleural to serum ratio of protein 0.67 and LDH greater than 2 /3 upper limit of normal for serum). Given the cost and logistic difficulties in obtaining LDH measurements and simultaneous serum protein specimens, an absolute level of the pleural fluid protein greater than 2.9 g/dL is often used in Uganda as an indicator of an exudative effusion. The lymphocytic predominance is typical for, though not
diagnostic of TB. In this case, based on the high pretest probability of TB and suggestive findings, empiric treatment is indicated.

Access to facilities for tissue and sputum culture are often limited in resource limited settings. In this case, the biopsy specimen was sent for culture as part of a research study. Culture was positive after 4 weeks.

**What is the role of chest tube drainage and decortication in patients with tuberculous empyema?**

The primary treatment for patients with tuberculous empyema includes drainage of the pleural cavity and early initiation of an appropriate regimen of antituberculosis medications. In centers with the capability of chest tube management, this often consists of placement of a pigtail catheter for drainage of the involved space. In a study published from Taiwan in 2008, in patients with loculated pleural effusions, use of streptokinase was found to decrease both time to improvement and the extent of residual pleural thickening at 12 months (Chung et al). Given that the large volumes of Streptokinase required and the lack of impact on disease cure rates or mortality, Streptokinase use is not standard practice in resource limited settings. Thorascopic decortication is also potentially of benefit, but is beyond the means of most centers in resource limited settings. Given the cost and the difficulty in management of chest tubes in Uganda, standard practice is to reserve chest tube placements for complicated effusions with air fluid levels and concern for tension pneumothorax. With or without decortication, with susceptible organisms, nearly all patients with tuberculous pleural effusions will respond to antituberculous medical therapy.

**Is he a candidate for antiretroviral therapy. What is the role of Antiretroviral Therapy in the treatment of his disease?**

The history that he was told he is not a candidate for ARV therapy by his outpatient clinic is surprising given his apparent state of significant immune compromise. Current practice in Uganda suggests that treatment is indicated for CD4 counts less than 200 or those with WHO stage IV disease. Based on both his CD4 count and his clinical staging, he would be a candidate for treatment.

In the context of tuberculosis disease, decisions regarding the timing of antiretroviral therapy are complicated both by the potential for drug-drug interactions between antiretroviral medications and medications given for tuberculosis disease as well as the potential for the acute worsening of symptoms due to increasing inflammation with immune
reconstitution. The rationale for early treatment is that in patients with very low CD4 counts, the risk of death from other opportunistic infections during the period of TB treatment is quite high. Reconstitution of the immune system may also facilitate the body’s intrinsic efforts to contain tuberculosis disease. Studies are currently underway to establish appropriate indications for early ARV treatment for patients with TB.

Current practice in Uganda and many settings is to defer treatment for HIV until the end of the initiation phase of treatment. In this context, it is extremely important that patients be educated regarding the need to follow up for HIV treatment as the risk of loss to follow-up is high. This is particularly true in settings where TB treatment is delivered in a setting separate from the HIV care programs.

**Is there any role for corticosteroids in the management of tuberculous empyema?**

The role of corticosteroids has been reviewed in multiple trials as well as Cochrane Collaboration systematic reviews (Cochrane 2007). Though there is some indication of an early 4 week decrease in fluid reaccumulation, these differences are not sustained at 8 weeks and do not appear to correlate with long-term outcomes including the extent of residual pleural adhesions. There is additionally a theoretical potential for harm in those with HIV in the form of an increased risk of development of Kaposi’s sarcoma. There is not sufficient evidence at this time to support the use of corticosteroids as adjunctive therapy for tuberculous empyemas.

**References:**

*In progress*
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Courtesy Tracy Rabin and Jeremy Schwartz

Plate 2
Oral Thrush
Courtesy Tracy Rabin and Jeremy Schwartz

Plate 3
Oral Kaposi’s Sarcoma
Courtesy Coeurlida Louis
Plate 4
Oral Kaposi’s Sarcoma
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Plate 5
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Plate 24

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Courtesy Elizabeth Kvach.

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Courtesy PENDING, Institute of Tropical Medicine, University of Antwerp

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Courtesy PENDING, Institute of Tropical Medicine, University of Antwerp
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Courtesy Erwin Van den Enden, Institute of Tropical Medicine, University of Antwerp

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Courtesy Erwin Van den Enden, Institute of Tropical Medicine, University of Antwerp.

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Courtesy Esi Nkyekyer

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Courtesy Jose Evangelista
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Hyperinflation and right sided infiltrate due to PCP

Courtesy Jose Evangelista
Section 3: Reflections

A 14 year old girl was brought to Mulago Hospital on a Thursday because she was coughing and feeling short of breath for the past 2 weeks. She and her parents offered little history. They denied fevers, sputum production, coughing of blood, weight loss, night sweats or other symptoms. In the emergency room, she was noted to be wheezing and was admitted for asthma. She was prescribed albuterol MDI and an x-ray was ordered before she was taken to the pulmonary ward.

A Yale resident rounding early Saturday morning on the nephrology ward was approached by a frantic mother who said her daughter was having trouble breathing. She said, “My daughter is dying.” Upon arriving to the bedside of the young patient, he noted a thin girl in severe respiratory distress. With the help of a Ugandan intern, he obtained the very limited history. He noted that the patient appeared small for her age. Her vital signs: respiratory rate = 40, heart rate = 120, blood pressure = 80/45. A pulse oximeter, found locked away in an office down the hallway, showed an oxygen saturation of 85%. She had central cyanosis. Her lung exam revealed rales on both lung fields but no wheezing. Her heart was tachycardic without murmurs or gallops. He did not appreciate pulsus paradoxus. The remainder of her exam was unremarkable. The x-ray from the day before showed an enlarged, globular appearing heart with diffuse bilateral pulmonary edema. The resident’s first impression was that the patient was in cardiogenic shock. With her severe hypoxemia, she was in vital need for supplemental oxygen. Unfortunately for the young girl, and the other patients on the pulmonary ward, oxygen had been unavailable for the past two days. And at the time, intubation and mechanical ventilation were not realistic options.

There is an extensive list of possible etiologies including valvular heart disease, congenital malformations of the heart such as the tetralogy of Fallot, and myocarditis. Though less likely given the presence of pulmonary edema and central cyanosis, the young girl could also have cardiac tamponade. In fact, of the many possible causes of cardiogenic shock, tamponade is one of the few that can be treated at Mulago. An urgent pericardiocentesis can potentially be life-saving. An echocardiogram was sought to rule out cardiac tamponade and to assess
her cardiac function as well as other underlying valvular or structural heart disease.

In Mulago Hospital, there are two echocardiogram machines. One is a remnant from decades past, among the first generation of portable ultrasound machines. The other one is a private machine owned by a local cardiologist. A desperate search through the hospital early that Saturday morning failed to locate the ultrasound, the cardiologist, or an attending physician to assist in the case. Every minute that passed would bring the girl closer to her death. The only option left was to transport the young girl to the radiology department, where ultrasound machines were used for abdominal ultrasonography and US-guided biopsies.

The young girl was hurried down to radiology in the arms of her desperate father, trailed by the Yale resident, the Ugandan intern, the patient’s mother and her 2 younger siblings. A Ugandan senior house officer (SHO) joined the entourage hoping to lend a hand. To everyone’s disappointment, there was no radiologist or technician immediately available. The team waited in the ultrasound suite while the young girl continued to gasp for air. Every breath seemingly more labored than the last. Knowing that time was not on their side, the Yale resident and Ugandan SHO tinkered with the ultrasound machine hoping to obtain some images of the young girl’s heart to rule out tamponade. Unfortunately, the machine did not cooperate. After some time, a radiologist finally came to their aid. A brief ultrasound exam did not reveal pericardial fluid. The radiologist had no prior training in cardiac ultrasonography, thus was not able to determine if the young girl had any underlying structural heart disease. Nor was he able to further assess the cause of her cardiogenic shock.

All that could be done at that point was to keep the girl comfortable, knowing that her death may be imminent. She was taken to another ward, where oxygen was available. A few other consultants, including a Yale attending physician and the cardiologist, evaluated the young patient later that morning. On the heart rhythm monitor the cardiologist noticed a possible delta wave and made the diagnosis of Wolf-Parkinson-White syndrome. He retrieved an ampule of amiodarone from his small collection of cardiovascular drugs and administered the drug to the young patient. Her heart rate and rhythm did not respond to the precious medication. The cardiologist then performed a bedside echocardiogram, which showed dilated cardiomyopathy and possible fibrosis of the right ventricle. Based on the findings, a preliminary
diagnosis of endomyocardial fibrosis (EMF) was made. However, many features of her disease were not consistent with EMF. The patient did not have ascites, which is a cardinal feature of this tropical disease, and EMF does not usually present with central cyanosis. EMF is a disease typically seen in the very poor. Cassava, a tuber that makes up the diet of many poor Ugandans, has been proposed as the causative factor in the development of this disease. However, this girl did not have a “positive” blanket sign – a term commonly used to describe poorer patients and their families who cannot afford a quality blanket to bring with them to the hospital. Her family members were well dressed in new traditional garments. It was unlikely that she came from a poor family.

A more detailed history from the young girl’s father, who spoke English very well, revealed that she had been “sickly” all her life. She had previous admissions for “breathing” problems. This new information made underlying structural heart disease as the cause of her cardiogenic shock more likely. Although the Yale attending and resident believed the clinical features did not support the diagnosis of EMF, they handed over the care of the patient to the cardiologist and his team. It would not have been constructive to have an open disagreement with this well-respected Mulago attending physician. The Yale resident later recollected that it was difficult to withdraw from this patient’s care, especially in light of a possible misdiagnosis. On the other hand, he questioned what really could be done to change the course of the young patient’s illness. He had to remember that although he was a contributing member of the ward team at Mulago, he was still just a visitor and had to respect the authority of the local senior physicians.

Like many other patients at Mulago Hospital with diseases in advanced stages, there was very little in terms of diagnostic or therapeutic interventions that could be offered to this young patient. Later that afternoon she was transferred to the cardiology ward for closer observation. After receiving a combination of minimally effective therapies, the patient remained on the cardiology service over the weekend with her family providing the most essential direct patient care.

On Monday morning, pulmonary medicine rounds were interrupted by a frantic intern from the cardiology service who sought assistance in the form of a pulse oximeter, additional manpower, and further clinical input. Given her quick pace and pressured speech, the pulmonary medicine team ran to the cardiology ward to find the 14 year old girl in severe respiratory distress surrounded by a team of interns and SHOs.
This was a Code in Mulago Hospital.

There were no nurses. There was no blood pressure machine. There was no telemetry. There was no crash cart. Her parents looked on at their dying daughter and a confused group of doctors. There was no code leader. The patient had gone apneic and did not have a pulse. An intern ran to find an intubation kit. Another began compressions on her fourteen year old chest. The senior cardiologist had arrived and brought with him a bedside echocardiogram revealing dilated cardiomyopathy with global hypokinesis. His clinical diagnosis remained EMF.

During this time, the patient was intubated by the senior pulmonologist, but no one had access to supplemental oxygen. She was bagged by another intern for some time, but transferring her to the vacant five bed Intensive Care Unit with decades old mechanical ventilators would be futile. Apparently, there was nothing more that could be done for this 14 year old girl. The patient received one round of epinephrine without effect. Still in pulseless electrical activity without a known reversible cause, the code was called. While in reality the code must have been minutes, to everyone there it seemed like an eternity. Instantly, the young girl and her untimely death became frozen in the minds of the Yale residents.

Mulago had sculpted Yale residents to become accustomed to differences in the style and practice of medicine. The Yale residents had to adapt and learn how to care for patients without the resources usually available to them. But the trauma of seeing a young girl without a definitive diagnosis being ineffectively coded, crossed a certain line. Unlike their Ugandan counterparts who were found to be resuming their daily rounds, the Yale residents were paralyzed. Most of them left rounds while word of the code spread throughout the hospital.

The senior attending physicians convened the large group of residents and medical students taking care of the young girl to review her case. The patient’s hospital course was outlined with responses from the senior attending physicians – whose careers had allowed them an in-depth clinical experience both in the United States and in resource limited settings. Uniformly they acknowledged this particular, emotionally gut-wrenching event, but went on to cite the high mortality rate at Mulago Hospital. A mortality rate that persists despite the hard work and dedication of so many people. The group went on to discuss the glaring differences between Yale New Haven and Mulago Hospital.
It was an unavoidable topic. But in the end the Yale residents had to be reminded that, for now, this was the reality at Mulago Hospital.

Laundry at the Hospital. Courtesy Klara Rosenquist

Circle of Silence
Katrin Sara Sadigh & Jeffery Luebbert

That first day the humidity took its hold of me and left me heady with exhaustion. The dark eyes of a marabou stork followed me into the hospital. I arrived early with the intention of getting my bearings and reviewing the recently admitted patients’ records. My white coat quickly signaled me out as the sole doctor, and a young girl ran towards me. She was no older than eleven or twelve, her voice urgent, her lips cowering over the words, “please, my mother she sick. Hell-ip, please hell-ip.” I was pulled as much by her as by a sense of responsibility, but I was quickly to find that this, along with many things at Mulago, was to be short-lived. The ward’s densely packed human bodies, filth and
stagnant air pressed upon me until my eyes were almost sightless by the time they found the young woman.

She lay on the floor between two beds, cachectic, her shallow breath catching in her visibly trembling ribs. I grabbed her chart—sheets of frayed loose-leaf paper stapled within colored construction paper—and read: “History of present illness: 28 year old female, with known HIV/AIDS, lacking antiretrovirals in her village, last CD4 count of 4, admitted one day prior with presumed sepsis, source possibly pneumonia.” She had received two antibiotics the previous night along with two liters of saline. Agonal breathing took hold of her, and her pulse rate began to slow. Feverishly, I ran through the ACLS protocol in my mind and asked the nurse for saline, atropine and epinephrine. The nurse appeared with a liter of saline and hung it from a hook on the wall. “Saline we have,” she started as she manipulated the woman’s IV. “But the others we have none.” I asked if there was a defibrillator. The nurse shook her head and walked towards another bed.

All at once I became aware of the girl who had not left my side. Her eyes cast about until they found the fear in my own. “She gets better, yes?” the girl asked. She accepted my lie. Climbing onto the bed alongside her mother, her small hand found its way into mine, while her mother’s faint radial pulse rested at my fingertip. We formed a circle and within it found peace. The woman died within minutes. Tears amassed beneath soft curves of lash and rolled off the girl’s face onto her dead mother’s body. She cradled her mother, and rocked her, gently humming. Before the wetness had dried on her face, the girl had already taken leave of her mother and stood before me. “Thank you,” she murmured into my white coat, her emotions a steady stream of tears mingling with my own. Words had long dried up and so I said nothing. I held her and then watched as she packed her mother’s few belongings, and walked out of the hospital alone, with soundlessness as inevitable as the marabou’s unflinching stare.
It’s unbelievable to see the end of this rotation approaching so quickly. This morning, Allison, my fellow med student, left for the airport and began her long journey home – odd how the thought of home is so comforting and yet quite foreign at the same time. Before Allison left, we three pioneering med students had a heart-to-heart with Dr. Sadigh, our advisor/roommate/mentor all rolled into one. At the time, all I had to say was how much I had immensely enjoyed and learned from the rotation. The truth, however, is that I am scared to leave. I feel like I’m on the cusp of a sweeping life change, but I don’t know where it will lead me. After all that Mulago has given me – motivation, perspective, a sense of justice, a new work ethic – what if I disappoint? What if this “potential” within me is wasted? How can I even begin to repay Mulago what I took this summer?

My experiences these past six weeks taught me that life is precious but so very cheap. My initial impression of Mulago was one of utter chaos. Patients die at an alarming rate: one third die in the hospital and two thirds die either in the hospital or within 2 months of discharge. Interns are so overburdened and poorly equipped that they are like firefighters using thimbles of water to put out the sun. Interns work for 6 months straight with zero days off and zero weekends, then get 2 weeks of vacation, then work 6 more months. On top of all this, it was absurd that the entire hospital was being painted sparkling new for the Queen of England’s November visit. As if investing in paint would improve patient care!

But there was order, however ludicrous, within the chaos. We kept a list of how much things cost at Mulago. The average Ugandan earns US$1/day (World Bank, per capita income US$280, 2005). Compare this to the prices of a complete blood count of US$3, chest x-ray of US$6, echo plus EKG of US$37, and mortuary services for body preparation of US$50. Certain medicines are free at Mulago so long as they are in stock. Outside pharmacies charge US$1 for metronidazole, US$5 for deworming treatments, and US$15 for Pepto-Bismol. As a medical student, I’ve always wondered how I could actually contribute to patient care. It was not until being in Mulago that I realized I could just hand
out money. Even so, the money I had in my pocket was a drop in the ocean of need…

I guess my greatest contribution was to one patient, SM. Mr. S was an impoverished 55 year-old man, past smoker, who had 6 months of increasing shortness of breath, occasional cough, and whole-body swelling. The workup included and was limited to 1) physical exam that revealed finger clubbing, tachypnea, bilateral wheezes, anasarca, and 2) bedside echo that showed right ventricular hypertrophy. Based on diagnoses of congestive heart failure and kidney failure, Mr. S was put on Cardiology, treated with free lasix and a nasal cannula to a communal, chronically empty oxygen tank. A chest x-ray order was written his first day of admission, and because Mr. S was so poor, the intern received approval to waive his chest x-ray fee. Unfortunately, Mr. S had no way of getting to radiology. He could not walk without getting short of breath and falling. He had no family or friends attending him. He could not afford to pay the US$3 bribe that hospital transport personnel charged to take patients around.

After 6 days of following Mr. S and waiting for a chest x-ray to get done, I had had enough. Apparently, there was no system in place to help poor patients with no attendants. I talked to 3 nurses, a radiology department receptionist, and an emergency room staff-member before I found Peter, who worked in the surgery emergency’s plaster casting room, who also had a key to the wheelchair storage closet. Then after wheeling my patient into 3 partly-functioning elevators to get Mr. S to correct floor, I had to clear the radiology receptionist, billing, and x-ray techs to jump the queue and get Mr. S’s long-awaited chest x-ray. Which showed Mr. S had TB! The next day, Mr. S was transferred to Pulmonology. The next week, after 3 positive sputum samples, Mr. S was moved to the TB ward to begin treatment. Mr. S’s first, only, and last English words to me – “Thank you, Madame” – only added to my tremendous sense of accomplishment.

When I then recounted this amazing success story to my brother on the phone, however, my brother asked quite simply, “Shouldn’t this be standard of care for every patient??”

July 29, 2007 – Sunday

I did not anticipate that coming back to the U.S. would be so unsettling and disquieting. I feel like everything and yet nothing has changed in
my life. My first email to Yale people still in Uganda said “I first noticed that: roads were too nice, people were too fat, people were too mean…” These reactions, along with sticker shock at the outrageously high prices of everything, were something I had expected. What I did not expect was the feeling of being lost, disconnected, unhappy, and angry.

Back in the U.S. only 4 days, I am hyper-critical of everything I see and everyone I interact with. I am thoroughly disgusted by so much waste, so much excess, and people being so clueless, ungrateful, and uncaring about others. Friends and family have already called me “misanthropic” because I find I have little patience for people’s problems here. When people ask how Uganda was, I only become more irritated. How could these people possibly understand all that I saw? I have constant flashbacks of roads that were more potholes than roads; of men bicycling towering mountains of plantains and pineapples for sale; of neatly-stacked pyramids of chipped battered skulls from genocide victims in Rwanda; of one skeletal, unattended, paralyzed patient reeking of urine and feces at Mulago on whom we practiced our neuro exam; and of a young orphaned girl, named Maska, that I played with at a roadside bus stop who rubbed her tummy and swallowed rocks to show me how hungry she was. Nothing I can say will change the lives of people in the U.S. Perhaps photos will show a glimpse of what life is like in Uganda, but I doubt even 10% of my experiences can be conveyed through pictures. I find myself wanting to either not talk about Uganda at all or take everyone I meet to Uganda to see life for him/herself.

After discussing my newfound negativity with family and close friends, I realize that my intense frustration stems in part from guilt and self-disgust. I see how privileged I am. In the eyes of every person I meet here, I see how oblivious I was before Uganda. Even after Uganda, I find myself inexplicably wasting time and money on irrelevant things. My inability to change myself also frustrates me so intensely!

Above all, I deeply miss being in Uganda; I felt so alive there. Those six weeks were hyper-stimulating in every aspect of life: food, culture, friends, classes, travels, and clinical medicine. Being in the U.S. is like life without color. I try to find solace in reminiscing to myself and with others who went to Mulago. And I try to use things I learned in Uganda: saying “Hi. How are you?” to everyone I meet, walking everywhere, critically questioning everything, and reading up on my clinical medicine.
So who should go to Mulago and Uganda in the future? Someone who is willing to be changed. Not someone simply wanting to go “experience Africa.” Someone oblivious, but not purposefully ignorant. Someone who can survive the despair and death to then see the beauty and lessons beyond. How about funding a group of three female med students from California, Michigan, and Illinois….

Excerpts of Journal Entries

Jeffrey Bigelow

April 24th 2007 (on the airplane flying to Uganda)

I anticipate this to be a life changing experience in a few ways:

1. Medically—I get to work at Mulago Hospital in Kampala, and am hoping to focus on the Neurology ward. This is going to be my exposure/debut hopefully to a lifetime career in international
neurology. There are going to be some fascinating neurological cases, most likely quite different from the states.

2. Understanding/sympathizing with humanity—I imagine this will happen in a couple of ways. I am going to see horribly sick, dying patients in the hospital. I’ve had some exposure to death, but this is going to be on a whole different level, and will be as a result of poverty. This is going to be hard and eye opening. We are going to see poverty in the cities and villages. Truth is it is there, and thus, exposure is important.

3. Cultural/geographical—Congo to the west, Sudan to the north, Kenya and Tanzania to the east, Lake Victoria and Rwanda to the south—a fascinating location! Anticipated activities include rafting on the Nile and trekking gorillas in the volcanic jungles of Rwanda. A unique, amazing experience just being there is going to be.

April 26th 2007

Finally saw Uganda in the light. It is very pretty—green spouts everywhere from every nook and cranny unless people stop it, the roads, even here in the city are red with mud, there are tons of huge birds. We are staying here at Lincoln Flat at Makerere University and this campus seems to be infiltrated with these huge 3 ft tall, 6 ft plus wing span stork-like birds with these huge gullets or something—they are otherworldly and made me think of the Dark Crystal. The city is a little overcrowded, poverty is present. Kampala is very similar to Accra and Port-au-Prince though maybe a little bigger, more metropolitan feeling.

April 28th 2008.

I’m writing this morning on behalf of yesterday, where I fell fast asleep with the intent to write—too sleepy to brush my teeth, read my scriptures, put my mosquito net around, or even get under a sheet. I paid with a couple of bug bites last night, hopefully none of those ridden with malaria.

So, yesterday at about 11AM I was taken over to Mulago Hospital and introduced to Fred who introduced me to Eddie and the team on the neurology ward. I joined their rounds for about 2 ½ hours where the intern would take the resident around to see the patients and then would scribe as the resident dictated his impression—kind of a slow process,
but I liked seeing the dynamic plan develop right in front of the patient. Bedside rounds are important though not very efficient—there’s probably a more happy medium towards how we do things at Yale and here. Lots of facial palsys. I was surprised to see old people and strokes. In the US, a stroke is an emergency requiring immediate intervention, where these patients had already been here a day or two and then we were talking about thinking about getting a CT scan. I guess emergent interventions like tPA aren’t available, so the rush is less emergent. A few cases of seizures. A young girl with a poorly defined weakness whose mother discharged her against medical advice because her other child had died the previous day due to “a fever.” Sad, especially because the mother wasn’t crying uncontrollably; she seemed resigned to that’s just how things are.

I then spent to afternoon/evening til about 10PM in casualty (which is not as bad as it sounds, just the name for the ER). The on-call team admits 30-60 patients per night which they then hold in a room and redistribute to the appropriate services in the morning, a different but efficient approach. Definitely patients are sick, no light admissions.

The most impressive thing was the residents. They are very sharp, well-educated, seem to be happy about working; they commented about the long day but didn’t complain about it. I was impressed with the valiant, continuous efforts to teach the medical students—even when it meant prolonging rounds at 9PM on a Friday night.

This is definitely going to be a month where I take a great amount more than I feebly give. I like that.

April 30th 2008

Today was a fine day. I’m very impressed with the residents, the attendings, and also the medical students at Mulago. They are very sincere in their work, dedicated, and I think a bit more thirsty for knowledge (though their base/fund is as good as most) than the average American resident, including myself.

The ward was interesting today—some very sick patients and lots of limitations due to inavailability of test in the first place, with inability for patients to pay anyway. Physical diagnosis is key. I want to hone that skill.
May 2nd 2008

I observed a couple lumbar punctures done by the interns today; they have treatment rooms they do the procedures in as the wards are very unprivate. The memorable (unsuccessful) LP was done on a very pretty, dainty young lady, quiet-mannered and shy, whose legs grew progressively weak to the point of paralysis and incontinence over a month, who they had finally got around to (the delay I believe was multifactorial). Her younger brother was “smartly” dressed in a striped-tie and plaid shirt and we lifted her onto the gurney, stripped her down to her waist (Was this embarrassing in front of her brother? If so, she didn’t protest) and then proceeded to the procedure with no anesthetic, partially sterile, and she didn’t make a peep and barely winced. Four unsuccessful sticks. I was impressed but noticed on the next stick peering into the deep hole of her crouched over body, her face was hiding pursed lips, eyes in pain, and a young girl trying her best to be brave. No lidocaine, very painful. The memorable part was right before we started another nurse came who was looking for the patient to break the news to her that she was “sero-positive” meaning newly-diagnosed HIV. They didn’t want to traumatize her with the procedure and the news at the same time, so the procedure won over. How much English did the girl or her brother speak? I’m not sure, but the intern and the nurse were talking about this in not-so-veiled terms in front of the patient. Kind of ironic how they were trying to sympathetically break news where I think the patient may have understood more than she let on, and that would have been a bad way to find out. I was saddened for this young girl getting this diagnosis. How was she exposed? How would others take it? Is this giving her a death sentence or does she have hope of getting antiretroviral treatment and regular medical care and living a semi-regular life? Maybe in the US, but I don’t think at this point that things go this way in Uganda, or Africa, or I guess the developing world. Kind of sobering.

May 10th 2008

The hospital is actually a very depressing place if I stop and think about it, though it is easy to not think about it and not feel depressed. The patients are so sick—so many of them are wasted down to skin and bones, are so malnourished and sick that they are apathetic, they barely move in their beds, change expressions, or make any noise at all. Many are beyond real care, whether they were here or at hospitals in the US.
It’s sad because appropriate, rather basic diagnostic tests are not done, sometimes symptom-relieving medicines foregone because the patient can’t pay. So, we know the appropriate intervention, it exists, even on the hospital premises. But it is a limited resource to be had for a price which often cannot be paid. For some of the bigger treatments/diagnostics there are a few ways to talk to social work and pursue things—but most of the small stuff, things essential for comfort, are not even presented as option.

I keep saying that in the US I think we overdo it sometimes, but here they often, almost always under-do it—there should be a happy medium, which maybe exists in Cuba or something. If I were a patient, I would rather have things over than underdone.

I hope that I can be more judicious of my use of resources in the US.

May 16th 2007

Nonsterile gloves, no anesthesia, reusing a needle, I guess this illustrates the frustrations that often exist working at Mulago. Today one of the heads of the Makarere University-Yale University Collaboration said Mulago had quite a heyday in the late sixties/early seventies when it was built, before the damaging reign of Idi Amin, and sounds like more advanced procedures, such as cardiac catheterization were taking place, when today they seem like a distant realization.

Mulago is a government run hospital poorly supported by the government. The housestaff are great and knowledgeable. In casualty (ER), they know exactly what should be done for emergencies for patients, but are unable to do it effectively or at all because the resources aren’t there, and especially because the patient’s can’t afford it. The hospital simply cannot just eat-up the cost as would happen in the US (at least as far as I’ve seen up to now), and as a result patients die.

For example, two people died last night. One came in, a known diabetic with a very high blood sugar, likely in diabetic ketoacidosis. This is a life threatening incident, but very common in the US and has a very set protocol of management. They don’t know why this lady died, but then told me that her electrolytes were never sent, that they were only able to take occasional blood sugars. Her family was involved and ready to pay, but labs aren’t readily (or at all) available overnight. This lady died and I’m convinced she wouldn’t have in the US. This isn’t because these
doctors didn’t know what to do; it’s that they didn’t have the resources available.

It’s a simple point/fact that has been in my face all month, I knew it would be before it came, but I wanted to try to illustrate it. It saddens me. It doesn’t make me want to run back to the US where we do absolutely too many tests. It’s just a sad illustration of the unequivocal distribution of resources in the world—again something I’ve seem before, am aware of, but I guess just wanted to vent about.

I really have given next to nothing during my month here. I love international work, am driven to do it and question what is the biggest benefit that I will be able to offer during my career? That is the question. Once I am a trained neurologist, will it be offering “my expertise” or is that presumptuous in assuming the recipient wasn’t well trained? Will it be offering collaborations with universities? Will it be offering supplies and manpower? Or is that just a bandaid effort and a waste or resources…or is the bandaid effort totally legitimate in the lives of people that actually do get helped? I am driven in this work, will continue to be, but my place isn’t straight forward. Many, if not most people doing so-called humanitarian work are very paternalistic, ethnocentric, egocentric in their approach.

These residents have definitely proved superior knowledge to mine in every way. But there is actually only one fellowship trained neurologist in the country. So maybe I will have an expertise and depth of knowledge worth sharing. I guess to me with my limited knowledge now, it seems presumptuous.

I have seen some wonder unique things on this trip. We are smack-dab in the middle of the world (have pictures at the equator) and in the middle of Africa. I’m so thankful to have had this opportunity. I never see right away how these experiences change/influence me, but I hope I have let it change/influence me in the way it should. Life is good. People are generous.
Journal Entries

Kaveh Sadigh

When one first sees the building of Mulago, it is hard to imagine that it is a hospital. It is beautiful in its architectural design, full of windows that constantly remain open, allowing fresh air to blow through the crowded wards. When the summer thunderstorms arrive, rain freely enters the corridors and slowly floods the floor until the hospital workers arrive with their mops and methodically wipe the floors, leaving behind thin traces of water that quickly evaporate in the equatorial heat. Family members crowd around the canteen, buying meat samosas, mutake, rice and African tea to bring back to the wards for their ailing loved one. Underneath this bustling activity that seems to fill the corridors of this hospital, there is quite another scene behind the double doors that separate the corridors from the medical wards that house the sick. That is where patients from all over Uganda lay, their lives interrupted by their various ailments.

It is behind these double doors where I have acquired some of the most memorable memories of my summer here, mainly through my interactions with patients and their families. There was Peter, the brother...
of the witch doctor who was admitted for Kaposi’s Sarcoma, who would contact me even after his brother was discharged. In the middle of the night, calling to ask for advice on how best to take care of his brother when he takes a turn for the worse, vomiting blood and the family not knowing where to go for help. When his brother died a few days later, he thought it worthy to call me and let me know of his passing.

There was Rose, one of my first patients at Mulago who had practically moved into the hospital with her family as she was being worked up for cancer. Her devoted husband was continuously by her side, her mother always on the floor organizing their cabinet and belongings as soon as she saw us, the muzungu doctors arriving to pay them a visit. And of course her beautiful toddler that was always playing by her side and would elicit a beautiful smile on her face...a universal smile all mothers have when they stare at their children...a smile so joyful and beautiful that it undermined the pathology that lies beneath it. And when we would try to speak Luganda to them with our scribbled notes from class, the laughter and amusement that it would stir in the entire ward as the patients watched the muzungu doctors try to stumble their way into their life and culture.

Then there was the patient with no family to take care of him, his bed in a corner completely isolated from the rest of the ward. And the kindness of a stranger who would pass his bed every morning as he went to the woman’s ward to look after his sick sister. This stranger, in the free time he had when not attending to his sister, took it upon himself to assume the responsibility of this forgotten man’s care. He would get his medications from the pharmacy and meticulously clean the phlegm drooping out of the dying patient’s mouth as if the man was his own brother.

Then the multitude of incidents that I would encounter...more often than I would like to admit, that has taught me the power of death and the complete helplessness of physicians to delay its coming. Like the morning on cardiology rounds when we encountered a patient in shock, no pulse, no blood pressure, shallow strained gasps that revealed how hard he had to fight to achieve each breath. His concerned family surrounded his bed, slowly retreating a few steps to make room for the doctors, hoping that something may be done for their loved one. There were no fancy gadgets with warning bells and whistles to interrupt the ward of the coming of death...to warn us of his falling pressure or pulse, to herald to the physicians the urgency of the situation. So when his turn came to be examined, death’s grip was too firm for us to convince Him
to be merciful. Before the right medication was found and retrieved from the pharmacy and the calculations for administering it were made...his shallow breaths had ceased. Death had won once again, leaving me humiliated at another loss. And once the realization had hit the family that he was lost to them, it only took a moment for them to remember the reality that is their lives and begin packing away their belongings to start preparing for the trip back home, where more responsibility and their routine daily work awaits them.

I know what my role is here at Mulago...a naïve student being a witness to the medical inequalities that plague the citizens of Uganda. But what is the role of the physicians here, who every day come to fight a fight that is becoming more and more difficult to win? They are the valiant warriors who stay on to fight even though they do not have the right weapons to ward off the enemy. But they do not abandon their post...when the enemy attacks them with machine guns they heroically fight back with spears. They do not abandon the people to fend for themselves. They stay to do what they can, be it making bedside rounds with an obsolete echocardiogram machine to provide a glimpse of a diseased heart, or providing symptomatic relief when no cure can be offered.

The lack of resources that the physicians have is quite evident to the westerner’s eye. The difference between the medical tools developed nations have compared to the dearth of resources Mulago Hospital works with is so great that the gap between these two nations borders on the absurd. One image that I will always carry with me is a particular morning that I was rounding with Professor Freer’s on the Cardiology service. As he was dragging his ancient, overworked echocardiogram machine with him from one patient to another, he noticed that there was a rip in the tube that connected the echo probe to the main device. The look of concern on his face was evident, as he gently held the newly defective piece in his hands not unlike a soldier who holds a newly wounded limb, lying limp at his side. He turns to look at me and sadly says “This is the beginning of the end.” His spear was now broken, and he had no replacement. There was a certain beauty in the way he took a piece of tape and gently sealed the rip, placed the probe back in its spot and dragged the echo machine on to the next patient. He continues his fight, with a mere piece of tape holding his spear together.

My time at Mulago has rapidly come to an end, and I leave having contributed very little to the health care at Mulago Hospital. In fact, I have grown more from the wisdom of the physicians and the kindness
of the patients than I would ever have thought possible. The endless number of patients willing to undergo yet another examination by this curly haired musungu contributed so much to my training as a future physician. Physical exam signs and X-ray findings that I had only read about in books the patients brought to life for me. Diseases that I have never even heard about, like Endomyocardial Fibrosis, now have a clear meaning to me, being permanently imprinted on my mind. Through time, my patients have become my mentors and my friends. They have given me much knowledge, kindness, and a new vision and strength. I now not only know more clearly my path in medicine, but my duty as a human being. I leave Mulago Hospital having witnessed the battlefield, now knowing clearly what I must do to arm myself for this fight. As I continue my training, I know that someday in the near future I will be back. Only next time I hope to contribute in a more substantial way to the citizens of Mulago Hospital, desperately trying to leave a mark on the community as large as the mark that they have left on me.
Making clinical rounds at Mulago evoked unforgettable images: the seemingly endless sea of suffering humanity; row upon row of ancient steel cots and mattresses strewn on the floor; the rusty IV poles and broken-down oxygen tanks; the smell of bleach used by cleaning staff desperately trying to keep up with the evidence of human waste. The impact of AIDS is devastating; these patients, who make up half of all admissions, filled the GI, Cardiology and Renal services and dominated the ever-expanding ID service which dwarfed all other services. There was the unforgettable look of pain, stoic suffering, dying on the faces of young and old alike, as they grappled with their very lives, caught in a system so bereft of basic medical resources. Patients and family members often had that look of resignation, accepting their fate because there was no recourse and life needed to move on.

I remembered this pervasive sense of hopelessness from my Resident days when I did an International Health elective in Tanzania. Many of the Yale residents at Mulago reacted to these circumstance with frustration and anger. At one point, Dr. Sadigh had to hold an emergency “summit” meeting so that everyone could vent and try to make sense of what seemed like a hopeless situation. Through the years, I have been conditioned to the ways societies function and I have learned that trying to fundamentally change the System in a sweeping and wholesale manner was futile, at least in the short run. I also knew that wallowing in despair and anger was fruitless. Perhaps unlike the residents, I have learned that change happens in small steps; one must start with oneself.

As an Attending, I felt more clinically adept. I was able to connect with the other Mulago Attendings who were expert clinicians. I admired Dr. Opio, a GI specialist, who, while rounding in a packed Casualty Ward, scanned the scene and singled out the one patient in marked respiratory distress in one corner of the room. Dr. Ochama adeptly triaged patients with acute abdomens into those whom surgery could benefit. I rounded with the venerable Dr. Szeze who pointed out uremic frost in an AIDS patient presenting with renal failure, something I had never seen before. But in turn, I felt I could contribute from my own medical experience: I
shared with Dr. Szeze that in the uremic AIDS patient, renal biopsy could show HIVAN and that in my experience, antiretrovirals could prove beneficial; he agreed to try this approach. In an elderly patient presenting with unexplained jaundice and renal failure, I suggested to Dr. Ochama the possibility of leptospirosis, and we started tetracycline. This Clinician-Clinician exchange proved rewarding and invigorating. I felt like I was part of a Guild — that we were able to communicate across cultural and socioeconomic divides; what united us was Clinical Medicine and the shared mission of saving lives.

After returning to the U. S., I was surprised by my own reactions to aspects of our medical system. I was dismayed by the tremendous waste of resources I observed. I consulted on a patient who had 20 negative blood cultures as part of a nosocomial fever work-up and I had flashbacks to Mulago where we could not obtain a single blood culture on the most septic of patients. I observed countless CT scans done on the same patient with headache and I had flashbacks to my Mulago patients, the lucky ones who scraped together all they had to obtain the CT that would discriminate which opportunistic infection they had. Here, physicians order such a plethora of tests that they lose sight of their significance. I observed myself and my colleagues spending inordinate amounts of time in front of computer screens, functioning as “data managers,” operating under the assumption that more data translated into better patient care. While I fully acknowledge the power of data in guiding clinical decision-making, I increasingly feel that our excessive focus on data creates a barrier between physician and patient. Pursuit of data creates an illusion of control and we can allow it to substitute for the healing inherent in our laying on of hands. We end up losing ownership of the patient and abdicate our central role in the healing process. The results of this approach are obvious: patients feel disconnected from their physicians, families can become antagonistic, and physicians feel disempowered, overworked and lose the sense of personal satisfaction. I asked myself, despite all these resources, were we better off than Mulago? Again, I felt the gnawing sense of powerlessness of being an individual clinician in an imperfect system that was much larger than myself.

Ultimately, we are products of our own socioeconomic and cultural environments. But, how do I make sense of the jarring juxtapositions between the two worlds I have been and are a part of? Is it possible to bridge the two worlds? On the one hand, Mulago is rife with example after example of patients dying due to lack of resources. Yet, back home,
we pour our wealth into the care of our patients, some of whom clearly benefit; but for so many, the results are marginal. Are our health outcomes proportionately better, given the scale of our resources? Are we optimizing the stewardship of such resources? Are we losing the satisfaction of practicing a healing art? Again, my guiding principle is that at least in the short run, I ultimately have control only of myself.

So, I began to ponder, what does it really mean to be an effective Clinician? From where does a clinician’s power ultimately derive? Clearly, we rely on our technical expertise, our knowledge of pathophysiology, our ability to use evidence to make diagnoses and formulate treatment plans. This is where judicious use of data can elevate us beyond the skills of healers trained in other traditions. But beyond this, I believe our power derives from our ability to listen, examine carefully, synthesize data and draw on our previous experiences. A good clinician is an amalgam of all of these—an Artesan who hones his skill and constantly adds to his toolbox. The transforming effect is obvious as the Clinical Artesan exudes confidence, and patients and families derive comfort and healing. This sentiment is expressed by Dr. Rachel Naomi Remen in her book, My Grandfather’s Blessing: “In a highly technological world, we may forget our own goodness and place value instead on our skills and our expertise. But it is not our expertise that will restore the world. The future may depend less on our expertise than on our faithfulness to life.”

I think back to my valiant colleagues at Mulago, how they struggle to be Clinical Artesans in a resource-poor setting and what a privilege it was to interact and learn from them. I think of all my past and current mentors who have valued the art of being a Clinician. I think of the future physicians, who are trying to find their balance within an often bewildering, technology-driven system. How do I teach and impress upon them the effectiveness and joy of honing Clinical Artesanship? I will close with an exhortation to all clinicians to test your clinical mettle at a place like Mulago. As summed up by Dr. Sadigh in The Heart of the Matter: “You are not a doctor if you can only function in a certain milieu...Sometimes, there’s just you and the patient.”
Uganda Observations

Andre Sofair

Traveling to Uganda and Rwanda after having been away from sub-Saharan Africa for two decades brought back many vivid memories mixed with new observations. Although my primary reason for travel was to supervise a medical student’s beginning her research project, I had the opportunity to work on the wards of Mulago Hospital and the time to take a weekend’s trip to neighboring Rwanda.

The first thing that struck me about the wards at Mulago was the immediate need of so many patients, many of whom traveled great distances at tremendous monetary and physical cost to be seen by a physician. On our ward, the vast majority of patients were stricken with the ravages of infectious diseases both acute and chronic (malaria, HIV, hepatitis B, or tuberculosis). In particular, the young patients with ascites or hepatocellular carcinoma from probable vertically transmitted hepatitis B disturbed me the most. Here were middle-aged adults, in the prime of their wage-earning years, many responsible for spouses,
children, and extended family, dying as the result an infection contracted as they were born and one that could have been prevented for a few dollars. Even so, these patients are so patient with the doctors and students who do their best to care for them within a setting that often allows only palliation. In cases such as these, I realize how much of life’s course is determined by where and to whom we are born.

My second observation was the pace at which our Ugandan colleagues work. Many faculty balance lives filled with research, teaching, and clinical responsibilities. Housestaff work without “caps” on patient admissions or restrictions on work hours in a clinical environment where ordering even the most basic tests (serologies or radiographs) is challenging. They do this day after day for very little pay and little prestige simply to follow their calling to care for sick members of their community. Watching the trust of these patients and the work ethic of these colleagues puts an added burden of responsibility on us, Western visitors who have been given so much by way of our birthright with little expectation the part of our hosts that we will give anything to them. Whether I am able to come back to help or contribute from afar, I must at least learn from their humility and grace to become a better colleague and physician back in my own country.

In Rwanda, I learned a great deal about forgiveness. Here is a country where just over a decade before, neighbors took up arms against each other in a country-wide genocide that took the lives of nearly 1 million people in only three months. Today, the legacy of this brutality is still evident, with many maimed citizens traveling the roads in wheelchairs or with crutches yet still able to greet me with a “bonjour” and a handshake of affection despite the personal tragedy that has befallen their country and their families. I wonder if I would be able to carry on after witnessing such cruelty that knew no bounds.

My voyage had a great impact on me and has hopefully given me the ability to be more patient, more kind, and more forgiving as I go through my daily life as a physician, as a parent, and as a friend.
My first day at Mulago Hospital began less than twelve hours after my plane landed. I received a very brief but enthusiastic orientation from a fellow student while walking briskly the hospital the next morning. Upon arrival, we headed immediately towards the infectious disease floor to meet up with the other students. I recall these first sights of Mulago well: the scaffolding, the front doors, the “keep Mulago clean” trash bins, and the eclectic lobby chandelier dangling precariously above our heads. We came soon to the floor. Pushing through the double doors to ward 4A and taking some nervous steps down the corridor, we were greeted by a near-synchronous turning of African heads. The patients and their attendants stared with expectant eyes at these ‘mzungus’ in white coats, as if we were there to do them some fantastic service. I froze. Whatever expectations I had going into the rotation were immediately gone. I knew then that the next month would be as unpredictable as it would be formative.

Traveling hilltop to hilltop from the familiar “Edgehouse” at Makerere University to Mulago was always transforming. During the twenty minute journey we each changed from being in Uganda to being of Uganda; from being guests to being clinicians. I thought I would welcome this change, but my presence on the wards served to bring out feelings of profound helplessness within me. Here we were, senior Yale students, armed with knowledge and experience among countless patients in need of our help, in need of someone to spend more than three minutes with them; but we were paralyzed by resource-poor setting. What could I do for the patient with advanced heart failure, no attendant, no blanket, no food, no money?

For a time I could not get past this. I distinctly recall my arrival on the wards one morning during the second week. Being greeted by that familiar turning of heads, hearing the coughs, seeing the frail, emaciated bodies overtaken by disease, I became completely overwhelmed. I nearly panicked. I just couldn’t take it – all the sick, dying patients and nothing I could do. The health care system in Uganda was simply not equipped to properly treat these people and there was nothing I could do about it. We were called later that day to a fortuitous meeting at the Yale-Makerere office. A Ugandan attending physician came to meet with us and offer his encouragement. While admitting that, medically speaking,
there was indeed very little we could do for the patients there, our attention to them and their families was an invaluable service. He was adamant that our taking time to care about them was more important than trying to solve their medical problems. Leaving that office I was more at peace finally having remembered my compassion and empathy, remembering that I could help by just being human. From then on, I did what I could for the patients. I dressed their wounds with the REMEDY supplies, shook their hands, held their babies, and accepted their laughs at my attempts to speak Lugandan. I remained profoundly impacted and troubled by their dire situations. That sadness never went away, but the frank humanity showed by the patients and our ability to connect inspired my daily return.

I have been a month back. People always ask me an oversimplified question, “How was Uganda?” All I can manage to say is that I am still digesting the experience. This is only partially true; I hesitate to talk in detail about the month because I find it difficult to adequately describe my time there. I want people to feel what I felt. The rotation has profoundly impacted me and the way I approach patients. Mulago showed me, very simply, the true face of the human spirit. Despite the supplies I brought and all the knowledge I gained, it was this encounter, this cultural exchange, that I believe was the most important part of being there.
It was early afternoon, we had just finished rounds on Pediatrics Ward C. Tomorrow was our day in the emergency room; I had never been there so I asked Carolyn to show me the area so I could get oriented. We walked down the intricate walkways of Old Mulago into a relatively deserted building (by now, all the new patients had been transferred to the wards and they still hadn’t accumulated new admissions). It was very nicely organized: the triage area on the left followed by the exam rooms where the doctors saw patients and then the admission area where those needing admission would receive initial bloodwork and treatment, awaiting evening rounds and the final decision to admit.

We were looking at the isolation room, where it seemed a neonate with tetanus had been placed to avoid the noise --the unmistakable rhesus
sardonicus (tetanus smile) on her unfortunate face. I remember us just starting to talk about how such things could be prevented by the vaccination of all pregnant women, that we were pleased to have participated in just such a vaccination campaign two days earlier. One of the Ugandan Senior House Officers (SHOs), frantic, ran up to us, “do you know how to use a defibrillator?” I was somewhat stunned, we were shocked. Rather than just replying, “yes,” I asked “why?” He wasn’t waiting around to give explanations. He shouted, “atrial fibrillation” and ran away into one of the other rooms. Carolyn and I looked at each other surprised? A defibrillator, here in Mulago? Here in the pediatric ward? For atrial fibrillation? I could count on my fingers the number of times I had seen a defibrillator used at Yale’s Children’s Hospital! By the time we came too and I decided we’d better check it out and figure out how we can help, he had disappeared. I too started running. I asked one of the other residents, “there was a guy here, talking about a defibrillator, where did he run to?” Thankfully, they replied in a surprisingly calm tone, “oh that was Mohsen, he’s in the Pediatric Intensive Care Unit (PICU).” They pointed us towards a room on the left. We took off our shoes and entered.

There she was, the unfortunate 6yr old girl, Amy, with critical aortic stenosis (and likely other unknown cardiac lesion) who had come in two nights ago with respiratory distress and found to be in heart failure. I remembered the long discussion during rounds today about whether or not to transfer her to the PICU. I remember being surprised at one of the SHO’s remarks, “what more can the PICU do for her that we can’t do here on the wards.” The answer, “well, they have an infusion pump so they can titrate the lasix drip.” I looked around the PICU – very clean, there were two nurses, the SHO, Amy, the infusion pump and I also saw a monitor similar to what we have at Yale, I remember being impressed. But then I realized the rhythm was not atrial fibrillation! “Does she have a pulse?” I asked suddenly. The SHO– Mohsen – felt for a pulse. He then looked at me, and before he or I could say anything, he started chest compressions. “Are you sure there is no pulse?” I asked again. He replied solemnly, “no pulse.” It was pulseless electrical activity (PEA) I was seeing on the monitor. I told the medical students to start bag mask ventilation and the other to get an IV for access. Thankfully there was a nurse in the room, as I called out for epinephrine. I turned around and realized the child’s beautiful mother was standing there not comprehending what was going on. She was escorted out of the room. We had done three rounds of epinephrine (realizing there was no bicarbonate or calcium gluconate or anything else for that matter to
give), we had given a good liter of normal saline. We still had PEA. Then I asked if the ventilator in the room worked, so that if we did resuscitate.... The resident looked down at his feet and said, “no-one knows how to use it yet.” We had just put this poor child through a resuscitation attempt... but to what avail? Even if we had restored a pulse, she would have needed to be intubated and ventilated as she was clearly unconscious. We had followed our medical reflex of running a “pediatric code,” without stopping to consider its consequences here at Mulago. Yet she was so young, in retrospect would we have done differently? At that moment it didn’t quite matter, we still had no pulse. Sweat was dripping from my brow as I continued chest compressions, these thoughts running through my head. I looked at the resident and explained it was time to “call the code.” The resident, “continue, I’ll get the attending.” The attending arrived, listened to the heart and exclaimed, “I don’t hear anything.” I closed poor Amy’s eyes and placed a sheet over her body. I said my own personal prayer under my breath. I turned to the nurse, she brought a screen around the child, and then they called in the mother. I still hear her wailing in the back of my mind. I had heard those cries so many times before at Mulago, somehow hers stung so much more. Tears welled up in my eyes. The attending and resident thanked us for our help. We stepped out of the PICU, put our shoes back on and walked out of the Pediatric ED.

Carolyn and I were silent on our way back through Wandegeya to our apartment. We contemplated what we had just experienced. A ventilator just sitting there... resuscitating to what avail... poor Amy.
It was only my second day in Uganda when I stuck myself with a needle.

Just one day earlier, I was assigned to the Infectious Diseases ward and was eager to make a difference. Among my initial observations was the senior resident departing the wards immediately after Rounds leaving a lone intern to perform the overwhelming duties of admissions, lumbar punctures, prescription writing, drawing blood and hanging IV’s.

The following day I sat down with the intern to determine how I could help. I then made a list of patients who needed procedures and blood work done; we ultimately decided I would help with the blood draws.

Later that morning, I slowly worked my way down the rows of patients with my cart. It had been a busy night of admissions and the ward was full. Since there were not enough beds available, many patients were lying on mats on the floor. Almost all of the patients on the ward had advanced manifestations of AIDS related infections. On Work Rounds it had appeared as if at least half the patients were suffering from cryptococcal meningitis including a stocky, young man in the middle row. Like many of newly admitted patients, he had learned he was HIV positive, or “sero-positive” (as these patients were often to) at the time of admission. He was uncomfortable from a severe headache and was sweating profusely.

Since there were very few butterfly needles, I was drawing his blood with a syringe and a straight needle. After drawing up a few cc’s of blood without difficulty, I glanced at the sharps container. This was actually a yellow cardboard box that was now overflowing with sharp used needles. While I was hesitating, a family was trying to make their way through some of the mattresses on the floor next to me to reach a relative. One of them tripped and fell into me, resulting in the syringe with attached needle puncturing my right index finger.

I am not sure what first ran through my head, but I remember having that horrible sinking feeling in my stomach. Almost in a trance I walked over to the nurse’s station, put the needle in an empty sharps container, took off my gloves, and stared at my hand. At the tip of my index finger, there was a small red spot under the skin, where I actually had injected a drop of the patient’s blood into my finger.
The intern noticed me looking at my finger and walked over to me. “You should probably wash your hands”, she remarked, immediately realizing what had happened. Otherwise I probably would have stood there forever. Robotically I walked to the sink and started washing my hands.

As I walked towards the lab one of the Ugandan residents I had met earlier waved at me excitedly. “How are you?” he asked. I told him about the needle stick. He put his hand on my shoulder. “I stuck myself three times already” he told me. “It is not a big deal here. You should probably go to the lab to get your blood drawn.” I felt a bit reassured until he added “I only know of one medical student and two interns here at Mulago that got HIV this way.”

I walked to the lab where the lab tech drew my blood. “Needle stick?” He shook his head and smiled “Oh-oh-oh. But this is life at Mulago Hospital. I am sure you will be fine”. As expected, my initial HIV test was negative.

I went to the cafeteria where Danielle, a fellow Yale resident was having lunch. “You should probably start the prophylaxis regimen.” she said matter-of-factly. “I actually brought my pills with me this morning” she added and handed me two pill bottles. Until Danielle reminded me, I actually had not thought about starting post-exposure prophylaxis (PEP). I took the yellow Kaletra pills and one yellow Truvada pill. As I read later that day, administering post-exposure prophylaxis decreases HIV transmission after needle stick by about 80%.

That same night I sifted through the big stack of papers and review articles in an apartment on the Makerere campus. I spent the next few hours reading an “Up-to-Date” article on needle sticks several times over. I found out less than a hundred cases of confirmed HIV seroconversions occured after needle stick injuries in the United States.

The next day I contacted Occupational Health at Yale New Haven Hospital. They were extremely helpful and arranged for another Yale resident to deliver the remaining 3 week supply of Truvada and Kaletra in a few days. I also spoke to Dr. Sadigh, the program director, who was extremely supportive and shared his own experience with needle sticks.

While talking with others was comforting, the next day I participated on Rounds, but avoided doing any procedures afterwards. Over the course
of the day a number of residents from Mulago informed me almost all the interns and residents had experienced needle accidents. Most of them had not taken the PEP medications; and if they did, only for a few days.

Kaletra and Truvada have a reputation as relatively benign medications, but after 24 hours I started developing worsening nausea. After a few days, the only food that did not immediately make me nauseous was the bland national Ugandan dish of matoke, a type of plaintain, which became the main staple of my diet.

A few days later, after a particularly busy day of admissions, the intern was drowning in work and procedures again. Reluctantly I agreed to help out by performing a few lumbar punctures, but I did not do any more blood draws while in Uganda.

Life went on at Mulago. The sheer amount of suffering at the hospital shifted my thoughts away from the needle stick to the task of caring for the many sick patients in the ward. While I rarely thought of the incident, the HIV meds and nausea were occasional unwelcome reminders. Talking to my wife was another reminder, and quite difficult at times, since I didn’t want to tell her over the phone what had happened, even though she clearly sensed something wasn’t quite right.

During my month of post-exposure prophylaxis I lost approximately 15 pounds. I also started developing some lipodystrophy including a “buffalo hump” and increased abdominal fat. I started counting down the days until my last dose.

After returning to Yale, I filled out an incident report with Occupational Health. Having my blood tested for HIV and Viral Hepatitis was a lot less anxiety provoking than originally anticipated. Several months later, after being informed that all tests were negative, my feeling of moving on was akin to crossing off a check box for a particularly difficult task on a resident’s daily to do list.

Looking back I learned two major lessons from this experience. First, percentages are not very reassuring when talking about a devastating disease like HIV/AIDS. While the probability of acquiring HIV through needle stick is low (less than 1%), even seemingly low probabilities can strike a dreadful feeling. Second, I learned physicians often minimize side effects. I recalled telling my clinic patients “You might experience some nausea and diarrhea” when initially prescribing medications. The implications of non life-threatening side effects such as gastrointestinal
symptoms, headaches, or lipodystrophy seemed hardly worth mentioning, especially when taking medicines intended to treat a potentially deadly disease. After enduring some of these “minor” effects for just a month, I have a newfound admiration for patients with chronic diseases like HIV/AIDS, who take these medications for life.

Uganda Chronicles

Esi Nkyekyer

It was mid-morning. The smells of freshly fried samosas, steamed matoke and simmering pea stew meandered upwards from the Good Samaritan Canteen, percolating the rawness of illness and suffering. A cool breeze whispered its way through the windows, swaying retired mosquito nets back and forth like pendulums in individual clocks of life. Some windows were only slightly open; others were ajar. So the pendulums did not undulate in unison. The breeze was comforting, akin to an attendant’s loving caress. Beyond the heavy glass from whence it came, the city of Kampala lived and breathed another day. Against the
backdrop of a cloudless blue sky, Marabou stalks in their majestic hideousness circled the land, cawing with ominous excitement.

‘Esi, could you please take this patient’s blood pressure?’

I had purchased my sphygmomanometer at the beginning of medical school along with other tools of physical examination – a stethoscope, a tuning fork, a reflex hammer. There is really no need for a personal sphygmomanometer in the United States; they exist abundantly in inpatient and outpatient settings alike. Furthermore, medical students and physicians rarely use these sphygmomanometers since nurses usually take patients’ blood pressures. Nonetheless, I dreamed that mine would be of great use one day, hopefully somewhere in Africa.

‘Absolutely!’

Measuring blood pressures of patients at Mulago hospital became a sacred ritual through which the unknown was revealed. The language barrier was such that, I usually had to gesture for patients to uncover an arm. Many were emaciated, reduced to the size and dependence of their childhood years, often requiring the use of a pediatric cuff. Sometimes their skin was dry and scaly, other times diaphoretic. Sometimes it was covered in lesions, other times as smooth and flawless as on the day of their birth. Sometimes it was fiery to touch, other times too cool for comfort. Despite these variations, their skin remained a constant testimony to their heritage - my heritage.

I positioned the cuff, then palpated for the brachial artery. No matter how faint, there was always a pulse, a reminder of life, a reminder of hope. As I inflated the cuff, with the bell of my stethoscope positioned over the brachial artery, I experienced a moment of calm knowing that the truth was imminent. I could hear my heart pounding in my ears. With the slow release of air, I listened beyond my own pulsations to the momentary silence of impeded blood flow – waiting as the dial of the manometer moved slowly counter-clockwise.

Africa is the continent of my birth. The blood that flows through you is the very blood that sustains me. With the first Koratkoff sound, the soul of Africa flows forth with liberated turbulence from its years of stifling oppression. It cannot contain its tumultuous story but gushes forward like all the water of the Nile through a tiny crevice. Pulsating. The rhythmic pounding slowly fades away as the noose unfurls. Then there is silence. Whoosh. Thump. Thump. Thump. Thump. Thump. Silence. What this absence of sound holds is not entirely clear. Perhaps the
quietness embodies hope of recovery from the wounds of time. Perhaps the promise of peace will resurrect as from the stillness of the grave. Whatever the case may be, the life force of Africa continues to flow through your arteries and veins. Unabated. It thirsts for freedom and justice.

‘His blood pressure is 128/70.’

It was hour 2 of morning rounds on the Pulmonology Ward, 4c. In the absence of frequently recorded vital signs or an established culture of pre-rounding, all data that informed patient care was obtained during rounds. It would take us at least 2 more hours to see the remaining patients on the ward – both male and female.

She was an HIV positive woman in her early thirties. Almost 90% of the patients on the floor had HIV. Their ‘status’ had become an integral part of their identity to us as medical students and personnel; it dictated what questions we asked next as well as any course of action we took in their care. Like many in her predicament, she wore her disease on her sleeve. ‘Olyotia nyabo (how are you doing madam)?’, we asked in Luganda. She looked at us with eyes set in deeply hollowed sockets and managed to smile, barely opening her parched lips. ‘Bulungi (good)’, she replied. Her prominent, high set cheek bones gave her a regal aura, belying the pain that wrought her entire abdomen. The freshly dried tear tracks, white and flaky against her velvety dark skin told it all. She lay very still. In polite Ugandan fashion she too asked us how we were, thus completing the daily choreography of greeting that maintained our connection as human beings.

Yesterday, we had wanted the patient to get an abdominal ultrasound as part of the work up to better elucidate the cause of her pain. Today we learned that the ultrasound had not been performed because she did not have an attendant to accompany her to the Radiology suite. An attendant is the patient’s most staunch advocate on the wards of Mulago hospital. This heroic figure is usually a relative or close friend who nurses the patient during their hospital stay. They often camp out on mats on the floor ensuring that their loved ones are bathed, fed, seen by the medical team, receiving their medications properly and completing all the diagnostic tests requested. It is as unfortunate as it is true to say that patients without attendants are often neglected and do not receive the care and attention that they so desperately need. We (the visiting medical students) decided to be her surrogate attendants by taking her downstairs for the ultrasound ourselves after rounds had ended.
It was not until after lunch that we returned to her bedside. At that time, we were relieved to learn that a cousin had arrived to assist her. She sat at the edge of the patient’s bed, bravely poised yet obviously worn with anxiety. Spread out on the faded and threadbare blanket were a few wrinkled Uganda shilling notes held down beneath piles of coins. Sunlight streamed in through the window casting a shadow of dancing leaves on the faces of the attendant and the attended. Down below, meticulously hand-washed sheets and clothing were spread out on the well-manicured grass, drying to a crisp in the breezy afternoon heat. They were 3000 Uganda shillings short of the 10000 necessary for an abdominal ultrasound. They were $1.50 short of $5.00.

I must have had at least 20000 Uganda shillings in my wallet. I hesitated. That period of momentary limbo is what I imagine judgment day will be like, with all the nervousness associated with the final verdict on one’s life. My gut reflex was to reach for my wallet and give them what they needed, heck to give them everything I had. My mind interceded. Is it really appropriate for me to offer these women money directly out of my pocket? What are the implications of such an act most especially when the recipients are so desperately in need? To be honest, I did not want to endure any untoward outpouring of gratitude from the patient for a service that should constitute a right and not a favor. Furthermore, I felt that as the giver, I would be creating an unnecessary hierarchy in which I, the ‘heroine’, was bestowing a kindness (that need not be considered a kindness) on an already vulnerable person - an individual fully deserving yet unjustly deprived. Selfishly, I did not desire to see myself in that position; I was perturbed by the ethical boundaries I felt I would be infringing upon. Yet only 3000 Uganda shillings separated this patient from a potential diagnosis.

I stared at the floor, looking up only occasionally to make temporary eye contact with my counterparts. We were silent but all obviously thinking the same thing. Charles, the senior house officer on our team, gathered the money on the blanket, counted it, and in his quiet emphatic manner said, ‘They are 3000 shillings short’. He looked each of us in the eye. I thought I caught a glimpse of accusation in his steady gaze; my own guilt was calling me out. With an air of tender despair Charles walked away and for a few minutes was nowhere to be found. He returned with 3000 shillings in hand, which he graciously gave to the patient’s attendant without much ado. I felt sick to the stomach, ashamed. All my angst
about whether or not it was ethical to give this patient money now seemed trivial and embarrassingly asinine…

Sacrifice. Here was a man with genuine love for his people, who selflessly desired to ease their plight, no matter the cost. I hold him in high esteem for the dedication, humble respect and sincere gentleness with which he approached all patients. A true pearl in his own right, Mulago hospital would be a different place if the majority of administrators and health care personnel were more like him.

From our tranquil abode on Makerere’s campus, I watch the sun as it disappears beyond the horizon. The sky glows brilliant hues of yellow, orange and red. Another day is drawing to a close. I savor every moment of the day’s happenings - remembering, re-feeling. My mind is intoxicated by the raw reality of life that defines this land. I desire to be a constant part of it. I yearn to give back to that which embodies and defines much of who I am. And I will.