



## **Introduction:**

Welcome to the clinical case-series, “Reasoning without Resources,” by Prof. Gerald Paccione of the Albert Einstein College of Medicine. These teaching cases are based on Prof. Paccione’s decades of teaching experience on the medical wards of Kisoro District Hospital in Uganda. They are designed for those practicing in low resource settings, Medicine and Family Medicine residents, and senior medical students interested in clinical global health. Each case is presented in two parts. First comes a case vignette (presenting symptoms, history, basic lab and physical exam findings) along with 4-10 discussion questions that direct clinical reasoning and/or highlight diagnostic issues. A month later, CUGH will post detailed instructors notes for the case along with a new case vignette. For a more detailed overview to this case-series and the teaching philosophy behind it, see [Introduction to “Reasoning without Resources.”](#) Comments or question may be sent to Prof. Paccione at: [gpaccion@montefiore.org](mailto:gpaccion@montefiore.org)

## **About the Author:**

I’m a Professor of Clinical Medicine at the Albert Einstein College of Medicine in the Bronx, New York, where my career has centered on medical education for the past 40 years – as a past residency Program Director in Primary Care and Social Internal Medicine at Montefiore Hospital, and global health advisor and program leader at the school. I’ve served on the Boards of Directors of Doctors for Global Health, Doctors of the World USA, and the Global Health Education Consortium. I spend about 3-4 months a year in Uganda working on the Medicine wards of Kisoro District Hospital which, like most hospitals in the world that serve most of the world's population, has (almost) no resources. "At the bedside", I teach Internal Medicine residents and medical students how to assimilate the elements of history, physical exam and epidemiologic probability into a diagnostic impression that, even without definitive testing, can lead to appropriate therapeutic strategies in the field.

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## Case 56: Rash in the Way

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A 12 year old boy is brought in by his concerned parents from the pediatric ward where treatment for malaria with a full course of quinine failed to work.

About a month ago the usually active boy began to seem listless and fatigued, sleeping longer than usual and not playing with friends after school. He lost his appetite and complained of pain in his belly. Two weeks ago his mother noted that his belly appeared swollen, and he was “hot” at night and then sweat after going to bed. When he began to have pain “all over his body”, in his “muscles and bones”, he was given Coartem for malaria by the local health center, without relief.

He continued to have fevers, chills and sweats and his parents brought him to the hospital where he was admitted to the Pediatrics ward. There he was again diagnosed with malaria, and this time treated with Quinine. After continuing to spike fevers through 10 days of therapy, he was transferred to the adult male ward for another opinion (there had been no doctor on the Pediatrics ward for 4 months).

On admission to the male ward, his mother said he had lost weight and his belly was swollen. The fevers were worse, and the body pain increasing. He had never had anything like this before, had always been active and healthy, and did well in school. None of his friends were similarly ill, nor were any of their other 4 children although all had had bouts of malaria before. The family farmed, and owned some cattle and goats, and a pig, and occasionally consumed milk from their cow and home-made cheese. The child helped in the fields after school and had no contact with pond or lake water. He had had no sore throat, skin rash, cough, chest pain, headaches or diarrhea. His urine and stools seemed normal. His parents were healthy, non-migrant locals, and monogamous.

**Physical Exam:** In no distress, appears small in stature, sitting in bed

BP 80/60      HR 106      T: 102.6 orally      RR: 18

Skin: fine punctuate mildly erythematous rash diffusely, face, neck, trunk, legs (when pointed out to mother, she agreed)

HEENT: normocephalic; eyes: conjunctiva/sclera, without petechiae, icterus;

Mouth: no thrush, tongue normal; ENT: normal, without exudates or erythema

Neck: no JVP/HJR; shoddy lymphadenopathy, < 1cm; thyroid normal;

Lungs: clear

Heart: normal PMI, S1, S2; no murmurs, rubs or gallups

Abdomen: distended, diffusely tympanitic without shifting dullness; non-tender, no guarding

Spleen: large, soft, descends 4 cm below costal margin

Liver: non-palpable, 7 cm span; no masses;

GU: normal penis, testes and scrotum

Musculo-skeletal: full range of motion, no overt pain; no joint swelling

Neurologic: normal CN, motor, sensory, reflexes, gait

**1. What is the “frame” of the case (the key clinical features the final diagnosis must be consistent with)?**

- 12 year old, previously healthy boy in Uganda
- 1 month of constitutional symptoms and fever (fever was noticed for 2 weeks, but probably present for a month)
- splenomegaly 4 cm in a small boy, soft
- subtle rash, punctuate, diffuse, mild erythema

**2. What differential diagnosis fits the above frame? What features of the diseases nominated are at odds with the frame?**

- typhoid fever (*S.typhi*, ubiquitous, water-borne): a month of symptoms is long for typhoid, the rash of typhoid “rose spots” is unlike this one - evanescent and early in the course of the disease
- brucella (livestock, milk): rash uncommon and not like this patient’s (~1-3%), and in one series from Spain, 1/560 had “true rash” due to the infection itself; described as macula-papular or papulo-nodular, ~30% with a purpuric element; on legs/trunk, spares face, palms, soles;
- Q fever (*C.burnetti*, livestock): rash in ~3%, usually shorter duration (but can last over a month rarely), splenomegaly not a prominent feature
- leptospirosis (spirochete, livestock): the long, indolent course is atypical but possible, there was no biphasic pattern or “immune phase” manifestations seen here which are common with leptospirosis;
- borrelia (spirochete, relapsing fever): is characterized by acute recurrences with high fever, not long indolent course; epidemic, not isolated cases
- EBV infection: absence of lymphadenopathy or exudative pharyngitis makes this unlikely
- other viral exanthem: prolonged course, but there are many poorly-characterized viral infections in Africa and the inflammatory multi-system involvement suggests this could be one;
- other: secondary syphilis (spirochete), primary HIV: not sexually active, significant splenomegaly without lymphadenopathy unusual for each;

The lab had no reagents, and was closed for the week (lab tech at a family wedding in Kampala, promising to return with reagents (!)).

The patient was treated for typhoid with ciprofloxacin. No response was seen. After 3 days of treatment, the rash began to desquamate, most marked on his face, neck and arms, not seen on his palms or soles.

### 3. Which diseases prevalent in Uganda are consistent with the evolution of the patient's rash?

- Desquamation is not seen in typhoid's "rose spots" (which are almost always invisible on black skin anyway), further discrediting the typhoid diagnosis;
- The rash brings into consideration microbes that produce exotoxins, such as streptococcal scarlet fever or staph/strep muco-cutaneous infections. (However, the rash of scarlet fever is concurrent with a "strep throat", and neither a sore throat nor any site of mucocutaneous infection was evident.)
- Rashes from rickettsia or viruses could desquamate, but rickettsial disease is unlikely clinically.

The child continued to spike fevers and have body aches. On about the 10<sup>th</sup> day on the ward, he was seen limping in from the lawn where he would usually sit with his younger ambulatory ward mates, and complained to his mother of increased right knee pain and a painful testicle. Exam revealed a slightly warm right knee with an effusion, but full range of motion with some discomfort; and a swollen scrotum and tender left testicle.

4. a) What is the final diagnosis? Describe its salient epidemiologic and clinical features.  
b) How does the desquamating skin rash fit?  
c) Where had the initial clinical reasoning erred?

a) The disease is Brucellosis: This vignette describes a child with a classic case of a disease with protean manifestations. Even that the illness didn't become "classic" until later in the course is "classic" for Brucellosis – which has both acute and chronic presentations, and potential focal involvement of every organ system.

*Brucella is a gram  $\ominus$  coccobacillus that lives in the reticuloendothelial system of domesticated animals, survives up to 2 months in soft cheeses made from goat's or sheep's milk and 6 months in damp cool soil, and is stable as an aerosol. Transmission is via drinking unpasteurized milk or through contact with infected animals: thus the child's exposure to raw milk and livestock fits well. The true global prevalence is unknown due to the inadequacy of diagnosis and reporting of a non-specific illness that often remits without therapy, and the true incidence is probably over 10-20 times that reported in most countries. It's a major public health problem in the mid-East, north Africa, western, central and southern Asia, in Mediterranean countries, and in pockets of Latin America and sub-Saharan Africa.*

*As an intracellular, reticuloendothelial pathogen that stimulates a granulomatous response in the human host, the time course of clinical disease can be acute, relapsing ("undulant"), or chronic. As in some studies, especially of populations with large families who share exposures and eating habits, for every index case there's a yet-undiagnosed case in the family with more indolent disease.*

*Even the "acute" form is more insidious and less severe than many other acute febrile illnesses, and patients don't usually present until the end of the first week of illness or later. Evening fevers and*

notable weight loss within 1-2 weeks are common; half have arthralgias or back pain as non-specific complaints.

If untreated, the disease may progress to the “relapsing” form (the “classical pattern of “undulating fever” described by Bruce) and/or focality which usually sets in after the first month. Focal symptoms of hepatitis, arthritis, uveitis or orchiepididymitis in young males are common, as is a non-focal “fever of unknown origin” (FUO).

Some cases become “chronic”, lasting for more than a year, presenting either as a “chronic fatigue syndrome” or as localized illness (e.g. spondylitis, uveitis), often without fever or systemic symptoms.

On exam, ~30% have splenomegaly and/or hepatomegaly; 10-20% lymphadenopathy; 50% develop bone or joint disease with corresponding symptoms - osteomyelitis, usually spondylitis, is more common in adults >40 years old; or peripheral arthritis, usually knee or hip (either via reactive or infectious mechanisms) or sacroileitis (unilateral) predominantly seen in young adults.

Orchitis is seen in ~5%, and usually is a delayed manifestation of disease that has been causing fever for a while. Fever is reported in nearly all with orchitis, and precedes the development of testicular symptoms in ~80%. The testicular symptoms of pain/tenderness are usually mild-moderate, and the urinalysis often benign. This presentation is quite distinct from the most common causes of orchitis, Chlamydia/gonorrhea or enterobacteriaceae, in which local symptoms predominate, fever is often absent, and prolonged fever never precedes pain.

The clinical “clincher” in this case is the unusual and specific combination of findings: brucella orchitis is common in prepubescent males in whom other causes are rare; 80% have fever and 50% have a history of myalgia/arthralgia preceding the development of orchitis; and a third will have monoarticular peripheral arthritis present nearly simultaneously.

When the lab technician returned from the wedding with reagents from the capital, the Brucella agglutination test was done, revealing a titer of 1:640 (>1:160 probable, and 1:320 definite for diagnosis).

b) The skin rash is probably not related at all to the Brucellosis. In reviewing the history again, it fit well with a delayed photosensitivity response to the Quinine given for malaria on the pediatrics ward, first very subtle and noticed by the male adult ward team on transfer from the pediatrics ward after about 10 days of quinine therapy. During his stay, the child was ambulatory, and sat outside daily.

c) The team was “thrown off” by the rash and the initial differential constrained by keeping “rash” in the diagnostic “frame” of the case. Yes, it was related to the underlying problem, but only indirectly – as an iatrogenic complication of the prior misdiagnosis and its treatment!

### **Suggested Readings:**

Gotuzzo, E. *Brucellosis in Principles, Pathogens and Practice* (2<sup>nd</sup> Ed). Guerrant, R.L., Walker, D.H., Weller, P.F. Churchill/Livingstone/Elsevier 2006

Pappas, G, et.al; Brucellosis *N Engl J Med* 2005;352:2325-36.

Franco, M.P, et.al, Human brucellosis *Lancet Infect Dis* 2007; 7: 775–86

Navarro-Martinez A, et al Epididymoorchitis Due to *Brucella mellitensis*: A Retrospective Study of 59 Patients *Clinical Infectious Diseases* 2001; 33:2017–22

Nickel JC Chronic Epididymitis: A Practical Approach to Understanding and Managing a Difficult Urologic Enigma *Rev Urol.* 2003;5(4):209-215