



# HOLY C.O.W.!

## IT'S...

Clinical Question of the Week #13  
September 22nd, 2008 through  
September 29th, 2008

Please e-mail your answers to Kuo, Tim, Wendy, and Kevin ([klian@mednet.ucla.edu](mailto:klian@mednet.ucla.edu); [tprovias@mednet.ucla.edu](mailto:tprovias@mednet.ucla.edu); [wsimon@mednet.ucla.edu](mailto:wsimon@mednet.ucla.edu); [kbreger@mednet.ucla.edu](mailto:kbreger@mednet.ucla.edu)) by 0800 on Monday, September 29th, 2008. The resident or intern with the most correct answers at the end of each month will receive a prize!

**Case:** A 25-year-old man presents to clinic for evaluation of fatigue and dyspnea. Over the past several weeks, the patient notes insidious onset of fatigue and generalized malaise, followed by the gradual onset of increased shortness of breath when he tries to exercise. He has not had any fevers, chills, night sweats, chest pain, or edema, but he notes that on a couple of occasions, he's had bleeding while brushing his teeth. Examination reveals slightly pale and thin man, normal cardiopulmonary exam, and shotty scattered small lymphadenopathy. Laboratory data is pending, but the peripheral blood smear is shown below.

\*\*This case was provided by Dr. Carl Schulze (UCLA IM '07), now practicing in Alice Springs in the Northern Territory of Australia – who made the diagnosis on the smear below.



### Questions:

#### 1. What is the diagnosis?

Acute myeloid leukemia, characterized by a clonal proliferation of myeloid precursors with reduced capacity to differentiate into more mature forms. The result is an accumulation of leukemic forms in the bone marrow, peripheral blood, and other tissues and a marked reduction in red cells, platelets, and neutrophils. Symptoms at presentation include weakness, fatigue, easy bleeding/bruising, and infections – all resultant from pancytopenia. Bone pain is infrequent, however, patients may also present with extramedullary involvement (myeloid sarcoma) of lymph nodes, mediastinum, intestine, epidural sites, uterus and ovary.

Fever, if present, is nearly always associated with an underlying infection, however rarely is due to the leukemia in the M3 acute promyelocytic variant. Skin may reveal petechiae, ecchymoses, or neutrophilic dermatoses. Fundoscopic exam reveals exudates or

hemorrhages, and gingival hypertrophy may be seen on oral exam. Lymphadenopathy is rare, as is hepatosplenomegaly. Rarely, patients may also present with symmetric or migratory polyarthropathy.

Laboratory evaluation reveals pancytopenia, neutropenia, with peripheral blasts that may be found in the peripheral circulation. Bone marrow biopsy reveals packed marrow with blasts but may also have extensive fibrosis. (0.5)

**2. What are the requirements for diagnosing this condition?**

Diagnosis relies on: 1) documentation of marrow infiltration; 2) identifying that the blast cells are of myeloid origin (via cytochemical or immunophenotyping studies, although a blast with an Auer rod is considered diagnostic – see below); 3) classification according to the FAB/WHO designation (traditionally the FAB series, which includes M0-minimally differentiated, M1-without maturation, M2-with maturation, M3-acute promyelocytic variant, M4-myelomonocytic, M5-monoblastic, M6-erythroleukemia, and M7-megakaryoblastic), each with varying prognoses; and 4) cytogenetic analysis to evaluate for specific chromosomal abnormalities associated with AML. (1)

**3. What is the key finding shown in the image?**

Auer rods (see arrow above), which are clumps of azurophilic granular material that form needle-like bodies in the cytoplasm of blast cells. They consist of fused lysosomes and contain large crystalline inclusions. They are also seen in pre-leukemic MDS with refractory anemia with excess blasts 2 (RAEB2). (0.5)

Auer rods are named after John Auer (1875-1948), who graduated from Johns-Hopkins Medical School, and subsequently studied the intracellular rods that came to bear his name, beginning with a case description of a young man who was admitted by Auer (then a resident) to Johns-Hopkins Hospital with infection and bleeding (to Sir William Osler's service, no less) – see what can come of writing a clinical vignette? One more day for the regional ACP!

**4. Name two adverse prognostic factors for this condition.**

In a study conducted by the German AML Cooperative Group, poor prognostic indicators included: 1) Age >60 years; 2) Bone marrow blast count  $\geq$  75% at diagnosis (relative); 3) Intermediate or unfavorable cytogenetics; 4) Absence of Auer rods (relative); 5) Serum LDH > 2.9 times normal; and 6) Failure to attain complete remission within 50 days. (1)