



HOLY C.O.W.!

IT'S...

Clinical Question of the Week #23
December 1st, 2008 through December
8th, 2008

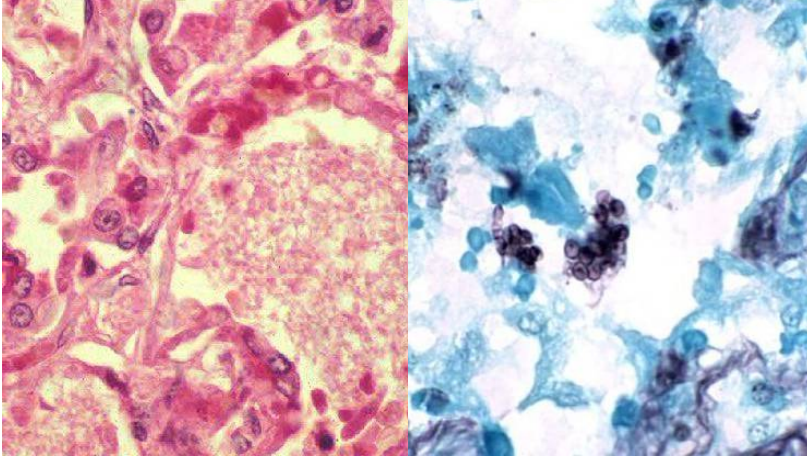


World AIDS Day is December 1st – raise some awareness! Please e-mail your answers to Kuo, Tim, Wendy, and Kevin (klian@mednet.ucla.edu; tprovias@mednet.ucla.edu; wsimon@mednet.ucla.edu; kbreger@mednet.ucla.edu) by 0800 on Monday, December 8th, 2008. The resident or intern with the most correct answers at the end of each month will receive a prize!

Case: A 28-year-old man presents for evaluation of progressively worsening shortness of breath. He was in his usual state of health until approximately two weeks ago when he developed insidious cough, intermittent fevers to 101°F measured at home, and increasing shortness of breath while walking. His past medical history is unremarkable, he doesn't smoke, and he lives with his partner in Los Angeles. Physical exam reveals temperature of 102°F, respiratory rate 20, and room air O₂ saturation of 89%. He is thin and weak appearing, oropharyngeal exam reveals few whitish plaques. Scattered crackles are heard on lung exam. CXR is shown below. Sputum is collected and images of stains performed are also shown.



The patient's chest radiograph.



H&E (left) and silver (right) staining of the patient's induced sputum.

Questions:

1. What is the diagnosis? What is the underlying condition?

Pneumocystis jirovecii pneumonia (i.e. the disease formerly known as Pneumocystis carinii pneumonia, PCP) is an opportunistic disease affecting severely immunosuppressed individuals, such as those in HIV/AIDS (the underlying condition in this case) with CD4 counts of less than 200. The PJ organism was first identified by Chagas and later Carinii in the lungs of guinea pigs in the early 1900s, and was first found in severely malnourished children in WWII. Recently, PJ was reclassified as most closely resembling a fungus, but taxonomy remains controversial – the new jirovecii designation now refers to the strain that affects humans (rather than carinii in rats).

Clinical manifestations include gradual onset of fever, dyspnea on exertion, progressive shortness of breath, fever, and tachypnea. Other symptoms may include chills, weight loss, fatigue, and chest pain. A minority of patients are asymptomatic. Physical examination reveals fever, tachypnea; lung sounds may be normal in half of patients, but crackles or rhonchi may be heard. (1)

This case was taken directly from a series of seminal articles in the New England Journal of Medicine in which the first patients with AIDS were identified, among whom several had PCP – 1) Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new cellular acquired immunodeficiency. **Gottlieb MS, et al. NEJM Dec 10, 1981;305:1425-1431. 2) An outbreak of community-acquired Pneumocystis carinii pneumonia: initial manifestation of cellular immune dysfunction. **Masur H, et al. NEJM Dec 10, 1981;305:1431-1438.** 3) Severe acquired immunodeficiency in male homosexuals, manifested by chronic perianal ulcerative herpes simplex lesions. **Siegal FP, et al. NEJM Dec 10, 1981;305:1439-1444.** Check them out – they offer a real and frightening peek into the initial discovery of the disease.

2. Name two other radiographic manifestations of this disease.

Radiograph of the chest may be normal in up to 25% of cases. Common x-ray findings include diffuse, bilateral, interstitial or alveolar infiltrates. Less common findings include pneumothoraces, cysts, nodules, lobar/segmental infiltrates, and pleural effusions. (0.5)

3. What is the treatment?

Anti-pneumocystis regimens include oral TMP-SMX (Bactim), TMP-dapsone, or clindamycin-primaquine for a 21-day course. Atovaquone may also be used. For seriously ill patients, IV TMP-SMX, clindamycin-primaquine, or pentamidine are used.

For patients who are found to have a PaO₂ ≤70mmHg or A-a gradient ≥35mmHg, corticosteroids are indicated. A standard 21-day regimen in use is as follows: prednisone 40mg bid for 5days, 40mg daily for 5days, and 20mg daily for 11days. (1)

4. Who is credited with the discovery of the causative agent in the underlying condition?

Initially, an American group led by Robert Gallo and a French group led by Luc Montagnier both claimed to have discovered the causative agent, the virus that came to be known as HIV. Later, it was conceded that Montagnier's group had the initial discovery, which was published in Science in 1983 (Barre-Sinoussi F, et al. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). Science 1983; 220:868-871), soon followed by the work of Gallo's group (Gallo RC, et al. Science 1984; 224:500-503).

In 2008, the Nobel Prize in Medicine went to Barre-Sinoussi and Montagnier for their discovery, along with Harald zur Hausen for unrelated work on HPV. Somewhat controversially, Gallo was not included among the honorees. (0.5) (Credit was also given to those who answered Chagas/Carinii/Jirovec for discovery of the PCP/PJP organisms.)

**For more, read the attached reflections of Robert Gallo on the 25th anniversary of the discovery in 2006, published in Retrovirology.