60. **Higenbottam T,** Jackson M, Rashdi T, *et al*. Lung rejection and bronchial hyperresponsiveness to methacholine and ultrasonically nebulized distilled water in heart–lung transplantation patients. *Am Rev Respir Dis* 1989;**140**:52–7.
61. **Oelschlager BK,** Chang L, Pope CE 2nd, *et al*. Typical GERD symptoms and esophageal pH monitoring are not enough to diagnose pharyngeal reflux. *J Surg Res* 2005;**128**:55–60.
62. **Potluri S,** Friedenberg F, Parkman HP, *et al*. Comparison of a salivary/sputum pepsin assay with 24-hour esophageal pH monitoring for detection of gastric reflux into the proximal esophagus, oropharynx, and lung. *Dig Dis Sci* 2003;**48**:1813–17.
63. **Bredenoord AJ,** Weusten BL, Timmer R, *et al*. Characteristics of gastroesophageal reflux in symptomatic patients with and without excessive esophageal acid exposure. *Am J Gastroenterol* 2006;**101**:2470–5.
64. **Bredenoord AJ,** Tutuian R, Smout AJ, *et al*. Technology review: esophageal impedance monitoring. *Am J Gastroenterol* 2007;**102**:187–94.
65. **Ravelli AM,** Panarotto MB, Verdoni L, *et al*. Pulmonary aspiration shown by scintigraphy in gastroesophageal reflux-related respiratory disease. *Chest* 2006;**130**:1520–6.
66. **Mainie I,** Tutuian R, Shay S, *et al*. Acid and non-acid reflux in patients with persistent symptoms despite acid suppressive therapy: a multicentre study using combined ambulatory impedance-pH monitoring. *Gut* 2006;**55**:1398–402.
67. **Tutuian R,** Mainie I, Agrawal A, *et al*. Nonacid reflux in patients with chronic cough on acid-suppressive therapy. *Chest* 2006;**130**:386–91.
68. **Hunt J,** Yu Y, Burns J, *et al*. Identification of acid reflux cough using serial assays of exhaled breath condensate pH. *Cough* 2006;**2**(1):3.
69. **Dupont LJ,** Dewandeleer Y, Vanaudenaerde BM, *et al*. The pH of exhaled breath condensate of patients with allograft rejection after lung transplantation. *Am J Transplant* 2006;**6**:1486–92.
70. **Krishnan A,** Chow S, Thomas P, *et al*. Exhaled breath condensate pepsin: A new noninvasive marker of GERD after lung transplantation. *J Heart Lung Transplant* 2007;**26**(Suppl 1):S139.


# Pulmonary puzzle

## Answer

*From the question on page 100*

Immunoassay for *Treponema pallidum* antibodies (TPAb ELISA) and the rapid plasma reagin test (RPR) performed at presentation were positive at high titres (1:16 and 1:128, respectively). TPAb were also detected in the cerebrospinal fluid (titre 1:128). *T pallidum* DNA-PCR of lung biopsy was not performed because of the poor specimen available.

Following the clinical and serological diagnosis of secondary syphilis with involvement of the central nervous system, intravenous ceftriaxone (2 g/day) was administered for 2 weeks because the patient reported allergy to penicillin. An unexpected and significant reduction in the major lung lesion was observed at the end of the antibiotic therapy and complete radiological disappearance of all pulmonary lesions had occurred at 3-month follow-up. TPAb and RPR titres both decreased to 1:8 after 3 months and RPR was negative at 6 months.

HIV/syphilis co-infection is associated with high rates of asymptomatic primary syphilis and with atypical features of secondary disease at presentation.[1] Lung involvement is extremely rare during secondary syphilis and it has been described mainly in patients with tertiary stage of the disease.

David and colleagues[2] recently reviewed nine cases published since 1967 which met the Coleman criteria for the diagnosis of secondary pulmonary syphilis (ie, physical findings of secondary syphilis, serological diagnosis, radiological lung abnormalities, exclusion of other forms of pulmonary disease and resolution of radiological abnormalities following anti-syphilis treatment).[3] Interestingly, eight of the nine patients had single or multiple lesions at lower lung regions.[2] Our patient with diagnosed secondary syphilis also had bibasilar lesions and alternative possible aetiologies for pulmonary lesions were excluded, both microbiologically and histologically. Even in the past when tertiary syphilis was not uncommon, one criterion to discriminate pulmonary syphilis from tuberculosis was the tendency of the former to attack the middle and lower lobes.[4] One explanation for the prevalent involvement of the lower lobes during pulmonary syphilis may be ascribed to the high oxygen sensitivity of the mircoorganism due to the absence of microbial enzymes that detoxify reactive oxygen species.[5] Despite its ability to spread in any tissue, *T pallidum* thus encounters an unfavourable environment in the lung. When pulmonary involvement occurs, it will conceivably take place in the less oxygenated area of the organ. The differential diagnosis for pulmonary nodules associated with cutaneous lesions includes a broad range of diseases (lymphoma, Kaposi sarcoma, metastatic malignancies, Wegener granulomatosis, sarcoidosis, mycobacteriosis, disseminated fungal infections and septic emboli); syphilis should also be added to the list.

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### REFERENCES


1. **Lynn WA,** Lightman S. Syphilis and HIV: a dangerous combination. *Lancet Infect Dis* 2004;**4**:456–66.
2. **David G,** Perpoint T, Boibieux A, *et al*. Secondary pulmonary syphilis: report of a likely case and literature review. *Clin Infect Dis* 2006;**42**:e11–15.
3. **Coleman DL,** McPhee SJ, Ross TF, *et al*. Secondary syphilis with pulmonary involvement. *West J Med* 1983;**138**:875–8.
4. **Morgan AD,** Lloyd WE, Prince-Thomas C. Tertiary syphilis of the lung and its diagnosis. *Thorax* 1952;**7**:125–33.
5. **LaFond RE,** Lukehart SA. Biological basis for syphilis. *Clin Microbiol Rev* 2006;**19**:29–49.