2. Humbert M, Monti G, Brenot F, Sitbon O, Portier A, Grangeot-Keros L, Duroux P, Galanaud P, Simonneau G, Emilie D. Increased interleukin-1 and interleukin-6 serum concentrations in severe primary pulmonary hypertension. *Am J Respir Crit Care Med* 1995;151:1628–1631.
3. Ogawa A, Nakamura K, Matsubara H, Fujio H, Ikeda T, Kobayashi K, Miyazaki I, Asanuma M, Miyaji K, Miura D, *et al.* Prednisolone inhibits proliferation of cultured pulmonary artery smooth muscle cells of patients with idiopathic pulmonary arterial hypertension. *Circulation* 2005;112:1806–1812.
4. Hashimoto K, Nakamura K, Fujio H, Miyaji K, Morita H, Kusano K, Date H, Shimizu N, Emori T, Matsubara H, *et al.* Epoprostenol therapy decreases elevated circulating levels of monocyte chemoattractant protein-1 in patients with primary pulmonary hypertension. *Circ J* 2004;68:227–231.
5. Perros F, Montani D, Dorfmuller P, Durand-Gasselin I, Tcherakian C, Le Pavec J, Mazmanian M, Fadel E, Mussot S, Mercier O, *et al.* Platelet-derived growth factor expression and function in idiopathic pulmonary arterial hypertension. *Am J Respir Crit Care Med* 2008;178:81–88.
6. Liakopoulos OJ, Teucher N, Muhlfeld C, Middel P, Heusch G, Schoendube FA, Dorge H. Prevention of TNFalpha-associated myocardial dysfunction resulting from cardiopulmonary bypass and cardioplegic arrest by glucocorticoid treatment. *Eur J Cardiothorac Surg* 2006;30:263–270.
7. Voisard R, Seitzer U, Baur R, Dartsch PC, Osterhues H, Hoher M, Hombach V. Corticosteroid agents inhibit proliferation of smooth muscle cells from human atherosclerotic arteries *in vitro. Int J Cardiol* 1994;43:257–267.
8. Mariette X, Brenot F, Brouet JC. Recovery from pulmonary hypertension with steroid therapy in a patient with Sjogren's syndrome and polymyositis. *J Rheumatol* 1994;21:772–773.
9. Kamata Y, Nara H, Sato H, Masuyama JI, Minota S, Yoshio T. Effect of steroid pulse therapy on mixed connective tissue disease with pulmonary arterial hypertension. *Ann Rheum Dis* 2005;64:1236–1237.
10. Kawamura N, Tsutsui H, Fukuyama K, Hayashidani S, Koike G, Egashira K, Abe Y, Yamamoto H, Tsuneyoshi M, Takeshita A. Severe pulmonary hypertension in a patient with systemic lupus erythematosus and minimal lupus activity. *Intern Med* 2002;41:109–112.
11. Ogawa A, Firth AL, Yao W, Rubin LJ, Yuan JX. Prednisolone inhibits PDGF-induced nuclear translocation of NF-kappaB in human pulmonary artery smooth muscle cells. *Am J Physiol Lung Cell Mol Physiol* 2008;295:L648–L657.

An Unusual Localized Progressive Fibrotic Cavity Mimicking Lung Malignancy in Idiopathic Pulmonary Fibrosis

To The Editor:

Idiopathic pulmonary fibrosis (IPF) is defined as a chronic fibrosing interstitial pneumonia of unknown cause limited to the lungs (1). Because of the increased risk in developing lung cancer, physicians must make their best efforts in their differential diagnoses of pulmonary cavities in patients with IPF. In this report, we describe a cavitary lesion resembling a cavitary mass in IPF histopathologically diagnosed as localized progressive fibrosis.

A 72-year-old man was admitted for further evaluation of a cavitary lung mass. Three years previously, the patient had been diagnosed as having IPF (Figure 1A) and treated with oral prednisolone and cyclophosphamide. On high-resolution computed tomography (HRCT) at 4 months before admission, a cavitary nodule 2.3 × 1.5 cm in size and 5 mm in wall thickness in the left upper lobe had been initially detected (Figure 1B). HRCT on admission showed a cavity containing a mural nodule 3.7 × 1.9 cm in size and 13 mm in wall thickness (Figure 1C). Contrast-enhanced CT of chest revealed an enhancement of the cavitary wall with suspicion of an aspergilloma or pulmonary tuberculosis. However, there was no evidence of infection of bacteria or fungus in sputum and bronchial washing fluids. Percutaneous transthoracic needle biopsy was performed. Histopathologic examination disclosed chronic inflammation with dense fibrosis, focal organization, and infiltration of neutrophils. On follow-up HRCT at 10 months after discharge, the cavity regrew to 2.7 × 2.6 cm (Figure 1D). The wall thickness of the cavity was increased to 18 mm, with a volume decrease in the involved pulmonary lobe. Moreover, diffuse ground glass opacity with diffuse honeycombing predominantly in the subpleural location was aggravated as compared with previous scans. Fluoroscopically guided percutaneous lung biopsy was performed again, but there was no evidence for infection or malignancy. A wedge resection was performed for the cavitary mass. Pathologic examination showed nonspecific chronic inflammation with dense fibrosis, and negative results of fungal and mycobacterial stains (Figures 1E and 1F). There was no evidence for recurrence through 20 months after the resection.

This is an interesting case of a pulmonary cavitary lesion histopathologically diagnosed as progressive fibrosis by repetitive biopsies, which could be misdiagnosed as aspergilloma or lung malignancy on serial HRCT. IPF is associated with an increased risk of various pulmonary diseases such as lung cancer, pulmonary tuberculosis, aspergillosis, and other respiratory infectious diseases. In addition, our case supports the existence of a rare entity, the localized progressive fibrosis presenting as cavitary lesions in IPF, although the prevalence is very low. Therefore, a pulmonary cavity with preexisting IPF should always carefully be evaluated and confirmed even though an invasive diagnostic modality may be used. The localized progressive fibrosis in our patient suggests that pulmonologists may include it in their differential diagnoses of cavitary lung lesions developed in IPF.

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Chi Ryang Chung, M.D.
Seoung Ju Park, M.D., Ph.D.
Kyung Hoon Min, M.D., Ph.D.
So Ri Kim, M.D., Ph.D.
Min Hee Lee, M.D.
Hyo Jin Han, M.D.
Kyoung Hwa Choi, M.D.
Gong Yong Jin, M.D., Ph.D.
Myung Ja Chung, M.D., Ph.D.
Yong Chul Lee, M.D., Ph.D.
Chonbuk National University Medical School
Jeonju, South Korea

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Reference

1. American Thoracic Society/European Respiratory Society. ATS/ERS International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. *Am J Respir Crit Care Med* 2002;165: 277–304.

Is the Reference Arterial pH Higher than Usually Acknowledged?

To the Editor:

Since the invention of the blood gas apparatus by Severinghaus and Bradley in 1959 (1), arterial blood gas analysis has become

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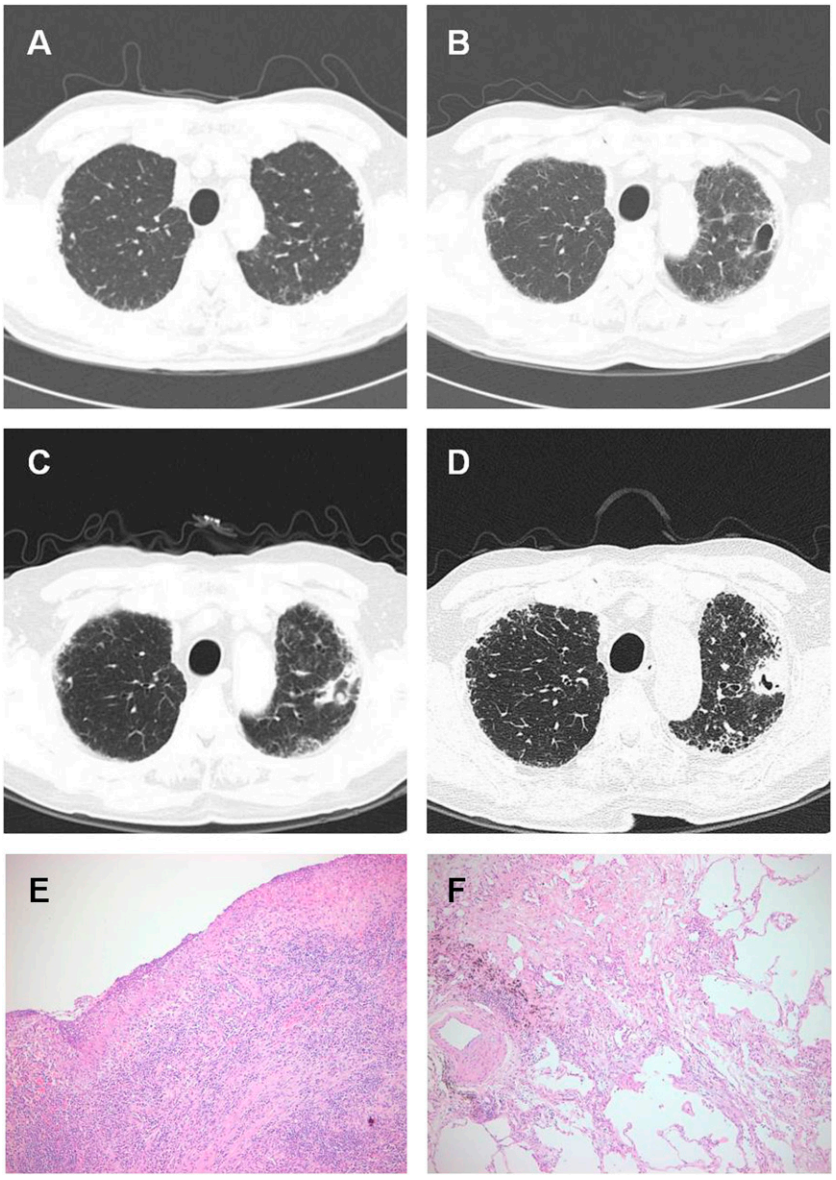

Figure 1. Chest computed tomography (CT) images (*A*) 3 years before admission, (*B*) 4 months before admission, (*C*) on admission, and (*D*) 10 months after a wedge resection. (*C*) High-resolution CT (HRCT) on admission showed a cavity containing a mural nodule 3.7 × 1.9 cm in size and 13 mm in wall thickness in the left upper lobe, suggestive of an aspergilloma. (*D*) On HRCT at 10 months after discharge, the size of the cavity was changed to 2.7 × 2.6 cm with 18 mm in wall thickness, suspected to be lung cancer. (*E* and *F*) Histopathologic examination of the resected lung specimen disclosed a nonspecific chronic inflammation with dense fibrosis (hematoxylin and eosin stain, ×100).

an invaluable tool in the clinical evaluation and management of patients with a wide scale of illnesses, particularly cardiorespiratory and nephrology diseases in emergency wards and intensive care units. Diagnosis and management of acid–base disorders in acutely ill patients requires precise and timely interpretation of the specific acid–base disorder, while delay in the diagnosis and therapy may be associated with considerable morbidity and mortality. Despite the importance and widespread use of arterial blood gas testing, accurate reference ranges, surprisingly, have not been established recently. The reference studies done in the late 1960s tested a numerically limited group of subjects, and in the last three decades hardly any study has been performed to determine the reference range for arterial pH. The most likely reasons for the scarcity of studies on arterial blood gas references, compared with studies that use venous blood samples, is that arterial puncture is more painful than venous punctures and that the risks for complications are higher. A single arterial puncture for blood gas analysis is very safe, but it may result in bleeding and hematoma formation.

Blood gases are now analyzed routinely on automated machines that use computer algorithms to adjust for system nonlinearities and inaccuracies. As a result, these machines most likely produce results considerably different from those of the manual instruments used in earlier studies. Also, most studies typically used only one analyzer model at a single study site, which ignores the small but statistically significant interinstrument and interlaboratory differences in blood gas measurements (2). The different reference pH values that are reported in the literature, therefore, will be related more to authors' preferences than to solid evidence. This is reflected by the wide variation in reference values published in several text books. As an example, five current text books published eight different "normal ranges" for the pH, varying from 7.35 to 7.40 at the lower level, to an upper level of 7.40 to 7.45 (3–7). Some textbooks even provide more than one reference pH value in the same textbook (6, 7), underscoring the uncertainty of these values. Different pH analyzer models may have statistically significant differences in pH values, but these differences are probably less than 0.01 (8). Acid–base reference values are further complicated by sex differences, and variation during the menstrual cycle will also influence the pH. Menstruating women exhibit a light but sustained hypocapnia during the luteal phase, with a decrease in Pa_{CO_2} of 3 mm Hg. The parallel drop in standard base excess may be up to 2.6 mEq/L and

[HCO_3^-] decreases about 2 mmol/L, resulting in an increase of pH of about 0.02 (9).

Recent arterial blood pH measurements in 221 healthy individuals, tested in several studies, consistently showed an arterial pH of 7.39 or higher, in some cases even up to 7.49 (2, 10–12). These pH values are higher than reported in most textbooks (4–7).

We need a better consensus because erroneous reference values may lead to potential overtreatment, undertreatment, or delayed treatment strategies when misdiagnosis is based upon an unjustified reference value.

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KENRICK BEREND, PH.D, M.D.
St. Elisabeth Hospital
Curaçao, Netherlands Antilles

References

1. Severinghaus JW. The invention and development of blood gas analysis. *Apparatus Anesthesiology* 2002;97:253–256.
2. Crapo RO, Jensen RL, Hegewald M, Tashkin DP. Arterial blood gas reference values for sea level and an altitude of 1,400 meters. *Am J Respir Crit Care Med* 1999;160:1525–1531.
3. Ratnam S, Kaehny W, Shapiro JI. Pathogenesis and management of metabolic acidosis and alkalosis. In: Schrier RW, editor. Renal and electrolyte disorders, 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2010. pp. 86–121.
4. McCool FD. Evaluating lung structure and function. In: Andreoli TE, Benjamin IJ, Criggs RC, Wing EJ, editors. Andreoli and Carpenter's Cecil essentials of medicine, 8th ed. Philadelphia: Saunders, Elsevier; 2010. pp. 198–212.
5. Stewart PA. Whole-body acid-base balance. In: Kellum JA, Elbers PWG, editors. Stewart's textbook of acid-base, 2nd ed. Amsterdam: AcidBase.org; 2009. pp. 181–197.
6. Halperin ML, Kamel KS, Goldstein MB. Fluid, electrolyte and acid-base physiology: a problem-based approach. Philadelphia: Saunders, Elsevier; 2010. pp. 9–59.
7. Bidani A, Tuazon DM, Heming TA. Regulation of whole body acid-base balance. B. Toews GB. Respiratory acidosis. In: Acid-base and electrolyte disorders. C. Whitney GM, Szerlip HM. Acid-base disorders in the critical care setting. In: DuBose TD, Hamm LL, editors. Acid-base and electrolyte disorders. A companion to Brenner & Rector's The kidney. DuBose TD, Hamm LL. Philadelphia: Saunders; 2002. pp. 1–22, 129–146, 165–188.
8. Hansen JE, Casaburi R. Patterns of dissimilarities among instrument models in measuring PO_2, PCO_2, and pH in blood gas laboratories. *Chest* 1998;113:780–787.
9. England SJ, Farhi LE. Fluctuations in alveolar CO_2 and in base excess during the menstrual cycle. *Respir Physiol* 1976;26:157–161.
10. Fan JL, Burgess KR, Basnyat R, Thomas KN, Peebles KC, Lucas SJ, Lucas RA, Donnelly J, Cotter JD, Ainslie PN. Influence of high altitude on cerebrovascular and ventilatory responsiveness to CO2. *J Physiol* 2010;588:539–549.
11. Hardie JA, Mørkve O, Ellingsen I. Effect of body position on arterial oxygen tension in the elderly. *Respiration.* 2002;69:123–128.
12. Mollard P, Bourdillon N, Letournel M, Herman H, Gibert S, Pichon A, Woorons X, Richalet JP. Validity of arterialized earlobe blood gases at rest and exercise in normoxia and hypoxia. *Respir Physiol Neurobiol* 2010;172:179–183.

Late Endobronchial Metastasis from Rectal Cancer that Mimics a Primary Lung Cancer

To the Editor:

Colorectal cancer is a common malignancy with a significant morbidity and mortality. Pulmonary metastases are rare (1–3%), and 10% of the metastatic cases present as an isolated pulmonary disease (1, 2). Therefore, the isolated pulmonary metastasis can be misdiagnosed as a primary lung cancer. Furthermore, because recurrence of colorectal cancer can be observed several years after curative resection, in the case of late pulmonary metastasis from rectal cancer, it can be difficult to distinguish it from a primary lung cancer.

A 67-year-old male was admitted to our hospital for evaluation of a solitary pulmonary nodule on chest X-ray. He had undergone a curative resection of rectal cancer 7 years previously. His smoking history was 50 pack-years. Computed tomography (CT) scan of the chest demonstrated a solitary round mass 7.0 × 2.0 cm in size, obstructing apical segmental bronchus, with an irregular margin and heterogenous enhancement in the right upper lobe and multiple mediastinal lymphadenopathies (Figures 1A and 1B). Bronchoscopic examination revealed a total occlusion of the right apical segmental bronchus by a polypoid mass (Figure 1C). Immunohistochemical staining revealed that the endobronchial mass was a metastatic rectal adenocarcinoma.

Colorectal cancer is the fourth most common malignancy in the world. The liver and lung are common metastatic sites, and usually occur within 2 years after curative resection of the primary cancer. Pulmonary metastasis of colorectal cancer usually present as multiple lesions in both lungs due to the distribution of the tumor via the circulation. However, approximately 10% of pulmonary metastases present as a solitary pulmonary nodule (3). Therefore, when a solitary pulmonary nodule is detected in a patient who currently has or previously had colorectal cancer, the suggestion of a metastatic carcinoma should be high. Quint and coworkers analyzed nodule morphology in patients with an extrapulmonary malignant neoplasm and solitary pulmonary nodule (4). The presence of mediastinal lymph node enlargement is suggestive of a primary lung cancer. Metastatic nodules are usually located in the lung periphery. In our patient, the margin of the nodule was irregular and spiculate and with mediastinal lymph adenopathy. Moreover, there was complete obstruction of the right apical segmental bronchus. These findings suggest that the nodule could be a primary lung malignancy. However, the histologic examination revealed adenocarcinoma cells positive for CK20, but were negative for CK7 and TTF-1, indicating that the nodule is a metastatic rectal adenocarcinoma.

Although the clinical presentation of our patient is atypical, the possibility of isolated pulmonary metastasis should be considered in patients with an endobronchial mass and history of colorectal cancer many years after curative resection.

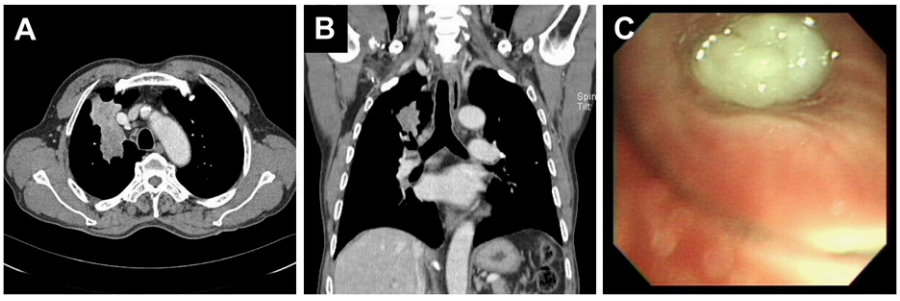

Figure 1. (*A* and *B*) Contrast-enhanced computed tomography scan of chest demonstrated a solitary round mass 7.0 × 2.0 cm in size, obstructing apical segmental bronchus, with a spiculated margin and heterogenous enhancement in the right upper lobe. (*C*) Bronchoscopic finding shows total obstruction of the right apical segmental bronchus by a polypoid mass covered with whitish necrotic tissues.