

## Rapidly progressive pleural effusion

JANUARY 2019

**TO THE EDITOR:** Regarding the article about a man with rapidly progressive pleural effusion by Zoumot et al in the January 2019 issue,<sup>1</sup> there was some inconsistency between the teaching points and the actions taken.

Question 1 asked what was the most likely cause of the patient's pleuritic chest pain. Pulmonary embolism was an unlikely diagnosis, given the patient's presentation and his normal D-dimer level, which the text acknowledges, but then proceeds to state that computed tomographic angiography of the chest was done anyway.

After pleural effusion was diagnosed, question 2 asked what was the best management strategy for the patient at that time. The best management strategy was to give oral antibiotics with close follow-up because the patient was at low risk of a poor outcome, but he was advised to be admitted for intravenous antibiotics anyway.

I'm not quite sure of the point of the didactic exercise when actions are not consistent with the analytic rationale for testing and treatment.

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### REFERENCES

1. Zoumot Z, Wahla AS, Farha S. Rapidly progressive pleural effusion. *Cleve Clin J Med* 2019; 86(1):21–27.

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**IN REPLY:** We thank Dr. Davidson for his comments. Indeed, the teaching points may appear inconsistent with the actual patient journey in this case. In the real world, physi-

cians from different teams and specialties are involved in the care of a patient, and medical practice may not strictly adhere to guidelines.

In question 1, the emergency department physician decided to proceed with computed tomographic pulmonary angiography to rule out pulmonary embolism. Based on best practice guidelines, pulmonary angiography was not indicated, as the clinical pretest probability of pulmonary embolism was low, supported by the patient's negative D-dimer test. When we wrote the article, as we already had the scan, we used it to support the learning points in terms of findings on computed tomography at the early stage of a developing empyema, and also to support that the scan was in fact not indicated (not the other way around).

As for question 2, specific data-driven guidelines do not exist on how best to manage patients with bronchopneumonia with an early evolving parapneumonic effusion. In the text that follows question 2, we stated that management as an inpatient or outpatient would have been reasonable. Although we considered the patient at low risk for a poor outcome, we offered inpatient admission at the time for better control of his severe pleuritic pain (this could have been made clearer in the text), as well as close monitoring of his evolving parapneumonic effusion, and we do not believe that this contradicts the teaching points of this case.

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## Metformin for type 2 diabetes

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**TO THE EDITOR:** I enjoyed reading “Should metformin be used in every patient with type 2 diabetes” by Makin and Lansang in the January 2019 issue.<sup>1</sup>

I just wanted to point out that metformin is a frequent cause of low serum vitamin B<sub>12</sub> levels, and serum vitamin B<sub>12</sub> levels should be monitored intermittently in patients using metformin.

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#### ■ REFERENCE

1. **Makin V, Lansang MC.** Should metformin be used in every patient with type 2 diabetes? *Cleve Clin J Med* 2019; 86(1):17–20. doi:10.3949/ccjm.86a.18039

doi:10.3949/ccjm.86c.04003

**IN REPLY:** We thank Dr. Moskowitz for his kind comments. We agree about the need for assessing vitamin B<sub>12</sub> levels during chronic metformin use.

Secondary analysis of patients in the Diabetes Prevention Program Outcomes Study showed a higher incidence of combined low and low-normal vitamin B<sub>12</sub> deficiency in users assigned to the metformin group compared with those assigned to the placebo group at the 5-year and 13-year marks after randomization.<sup>1</sup> Post hoc analysis of patients in the Hyperinsulinemia: the Outcome of Its Metabolic Effects trial also showed lower levels of vitamin B<sub>12</sub> and higher levels of methylmalonic acid associated with significant

worsening of a validated neuropathy score in metformin users.<sup>2</sup>

The mechanism behind the development of vitamin B<sub>12</sub> deficiency is not completely understood but could possibly be alterations in intestinal mobility, bacterial overgrowth, or calcium-dependent uptake by ileal cells of the vitamin B<sub>12</sub>-intrinsic factor complex.<sup>3</sup>

Our electronic medical record has a built-in tool that suggests checking vitamin B<sub>12</sub> whenever a patient requests metformin refills. There are no current guidelines on the need for baseline testing of the vitamin B<sub>12</sub> level. The American Diabetes Association recommends periodic measurement of vitamin B<sub>12</sub> levels, possibly yearly, in metformin users and more often if there are symptoms indicative of deficiency.<sup>4</sup>

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1. **Aroda VR, Edelstein SL, Goldberg RB, et al; Diabetes Prevention Program Research Group.** Long-term metformin use and vitamin B12 deficiency in the Diabetes Prevention Program Outcomes Study. *J Clin Endocrinol Metab* 2019; 101(4):1754–1761. doi:10.1210/je.2015-3754
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3. **Liu KW, Dai LK, Jean W.** Metformin-related vitamin B12 deficiency. *Age Ageing* 2006; 35(2):200–201. doi:10.1093/ageing/afj042
4. **American Diabetes Association.** 9. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes—2019. *Diabetes Care* 2019; 42(suppl 1):S90–S102. doi:10.2337/dc19-S009

doi:10.3949/ccjm.86c.04004