glucose level of <80 mg per deciliter [<4.4 mmol per liter]) and the mean venous oxygen saturation was 80±10% (normal value, 65 to 70%). Three patients (18%) died in the hospital.

In line with these findings, the patient presented in the case had an initial blood glucose level of 116 mg per deciliter (6.4 mmol per liter), venous partial pressure of oxygen of 73 mm Hg, and a good clinical course.

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No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc1310560

THE DISCUSSANT REPLIES: Consistent with the comments by Goldman and Shtaynberg, methanol or ethylene glycol toxicity cannot be ruled out exclusively on the basis of a narrow osmolal gap. After initial exposure to these alcohols, the osmolal gap may decrease over time as parent alcohol is converted into other metabolites and hydrogen ions, leading to changes in the anion gap. This patient's multiple-organ involvement, lactic acidosis, and negative toxicologic screening make such alcohol toxicities less likely. Whereas fomepizole is usually well tolerated, data to support its use are inconclusive.[1]

Korzets et al. are correct that thiamine deficiency can lead to lactic acidosis.[2] The gastrointestinal thiamine-deficiency syndrome, known as "gastrointestinal beriberi" and manifested by nausea, vomiting, and severe abdominal pain prompting laparotomy, has been reported[3] and could have been considered as a potential differential diagnosis for this patient. Nevertheless, her gastrointestinal symptoms were probably from pancreatitis resulting from metformin toxicity.

As stated in the Case Record, on respiratory compensation of metabolic acidosis for each 10 mmol per liter decrease from normal in the serum bicarbonate level, a compensatory decrease in the arterial pCO_2 of at least 12 mm Hg is expected. The decrease in pCO_2 of 1.2 mm Hg for each millimole-per-liter reduction in the serum bicarbonate level begins within minutes. Berend asserts that the use of this approach is misleading and suggests that the traditional Winters' equations should be used. Whereas these different formulas usually yield similar results, there are no convincing comparative studies of which formula is more accurate. Nevertheless, the delta approach, recommended in contemporary medical literature, is useful in other acid–base disorders. For instance, in metabolic alkalosis with adequate respiratory compensation, for each millimole-per-liter increase in the serum bicarbonate level, pCO_2 should increase by 0.7 mm Hg. In severe metabolic acidosis, there is a limit to the maximum respiratory compensation; for example, if the serum bicarbonate level is below 5 mmol per liter, the pCO_2 rarely, if ever, goes below a range of 10 to 15 mm Hg.[4] As stated in the Case Record, a part of the anion gap is probably related to severe hyperphosphatemia.

The statement by Protti and Gattinoni that hypoglycemia is not the rule in metformin overdoses is accurate. It is possible that the patient's venous oxygen content was not low because of mitochondrial respiration block caused by very high metformin exposure or because of severe acidosis itself.[5] Whereas this patient had a favorable outcome, metformin overdose should still be considered a potentially lethal event.

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No potential conflict of interest relevant to this letter was reported.

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