An 82 year old woman was admitted with worsening dyspnoea. Arterial blood gases were taken on air and revealed a pH of 7.39, with a partial pressure of CO₂ (pCO₂) of 1.2 kPa, pO₂ of 19.3 kPa, HCO₃⁻ of 13.8 mmol/litre, and base excess of −16.3 mmol/litre: a compensated metabolic acidosis with hyperventilation induced hypocapnia, which is known to be a feature of lactic acidosis. There was also an increased anion gap ((Na⁺140 + K⁺4.0) − (Cl⁻ 106 + HCO₃⁻ 13.8) = 24.2 mEq/litre (reference range, 7–16)), consistent with unmeasured cation. Lactate was measured and found to be raised at 3.33 mmol/litre (reference range, 0.9–1.7). After exclusion of common causes of lactic acidosis, Atorvastatin was stopped and her acid–base balance returned to normal. Subsequently, thiamine was also shown to be deficient. The acidosis was thought to have been the result of a mitochondrial defect caused by a deficiency of two cofactors, namely: ubiquinone (as a result of inhibition by statin) and thiamine (as a result of dietary deficiency).

An 82 year old woman was admitted after six weeks of worsening dyspnoea. She was breathless at rest and unable to carry out her normal daily activities. She reported no fever, cough, chest pain, or orthopnoea. She had a history of chronic obstructive pulmonary disease, mild hypertension, and had suffered a deep vein thrombosis 12 months previously. Drug regimen on admission was hypertension, and had suffered a deep vein thrombosis. She had a normal white cell count and no other inflammatory markers were demonstrably absent on a full blood count.

Arterial blood gases (ABGs) were taken on air and revealed a pH of 7.39, with a partial pressure of CO₂ (pCO₂) of 1.2 kPa, pO₂ of 19.3 kPa, HCO₃⁻ of 13.8 mmol/litre, and base excess of −16.3 mmol/litre: a compensated metabolic acidosis with hyperventilation induced hypocapnia, which is known to be a feature of lactic acidosis. There was also an increased anion gap ((Na⁺140 + K⁺4.0) − (Cl⁻ 106 + HCO₃⁻ 13.8) = 24.2 mEq/litre (reference range, 7–16)), consistent with unmeasured cation (lactate). This was thought probably to be contributing to her dyspnoea and a cause was sought. She was on no medications that are known to cause a metabolic acidosis and was not known to be diabetic, with normal blood glucose readings. Her renal function was good (admission creatinine, 118 µmol/litre (reference range, 30–110)), but her estimated glomerular filtration rate was decreased at 26.6 ml/minute (calculated by Cockcroft and Gault equation) and her liver function tests showed no rises in transaminases or bilirubin. Lactate was measured and found to be raised at 3.33 mmol/litre (reference range, 0.9–1.7). The patient was not hypoxic because her ABGs on air showed acceptable pO₂, and she was not clinically septic. Furthermore, she was not diabetic and was therefore not on oral hypoglycaemic agents, which have been associated with lactic acidosis (especially biguanides—phenformin—which is now withdrawn from use). A more obscure cause for her lactic acidosis was looked for.

Normal sodium and potassium values on admission (Na, 139 mmol/litre; K, 4.0 mmol/litre) were thought to exclude a renin–aldosterone axis cause (specifically hypoaldosteronism). Renin (4.1 nmol/litre/h (reference range, 0.76–3.2 erect)) and aldosterone (1041 pmol/litre (reference range, 110–860 erect)) were mildly raised, but these values were felt to be consistent with her diuretic treatment. Vitamin D (25-OH cholecalciferol) was normal: 24.5 µg/litre (reference range, 0.9–1.7). The only likely remaining causes were a metabolic myopathy and thiamine deficiency. It is well known that statins can cause myopathy and thiamine deficiency.2 The patient was taking Atorvastatin at 10 mg/day. This was stopped and she immediately improved clinically. Her ABGs and lactate values repeated one week later revealed pH 7.44, pCO₂ of 3.9 kPa, pO₂ of 10.8 kPa, HCO₃⁻ of 22.3 mmol/litre, and base excess of −3.9 mmol/litre. Her lactate had returned to normal at 1.71 mmol/litre. Her dyspnoea was also moderately improved. Therefore, it was possible that the lactic acidosis was related to the statin treatment. Six weeks later, the results of red cell transketolase enzyme activity became available: transketolase 0.65 U/g haemoglobin (reference range, 0.42–1.12), with a > 50% increase in activity when thiamine was added to the assay reagent (reference, < 25%), indicating frank thiamine deficiency. She was therefore started on thiamine treatment at this time.

**Abbreviations:** ABGs, arterial blood gases; bd, twice daily; coQ₁₀, coenzyme Q₁₀; HMGCoA, hydroxymethylglutaryl CoA; od, once daily; qds, four times daily; P, partial pressure.
DISCUSSION
We have reported an unusual case of lactic acidosis that appeared to resolve as a result of cessation of statin treatment. Possible causes for lactic acidosis included thiamine deficiency, vitamin D deficiency, myeloma, or abnormal renin–aldosterone functioning. It was later found that thiamine deficiency was also present and this may have acted in tandem with the statin to cause lactic acidosis, when neither element individually would have been sufficient.

Statins work by inhibiting hydroxymethylglutaryl-CoA (HMGCoA) reductase, but in addition to reducing cholesterol synthesis there is a decrease in the production of other non-sterols, such as coenzyme Q10 (coQ10: ubiquinone), and HMGCoA reductase inhibitors have been shown to reduce coQ10 concentrations. CoQ10 is an essential carrier in the mitochondrial respiratory chain that participates in oxidative phosphorylation. Consequently, there is decreased activity of mitochondrial complex I with inadequate substrate (acetyl-CoA and α-ketoglutarate tricarboxylic acid cycle effect) and reduced electron carrier transport (coQ10 effect) and mitochondrial function: effects of HMG-CoA reductase inhibitors on serum lipids. Thus, both statin treatment, via decreased coQ10, and thiamine deficiency, via reduced α-ketoglutarate dehydrogenase complex activity, can result in impairment of mitochondrial oxidative phosphorylation. It is possible that the lactic acidosis was the result of the combination of both thiamine deficiency and statin treatment, such that removal of one element was sufficient to resolve the metabolic stress and result in the resolution of acidosis.

Take home messages
- We report an unusual case of lactic acidosis thought to be caused by a mitochondrial defect resulting from a deficiency of two cofactors: ubiquinone and thiamine
- The deficiency in ubiquinone was a result of inhibition by treatment with Atorvastatin and the thiamine deficiency was dietary in origin
- When treatment with Atorvastatin was stopped the patient’s acid–base balance returned to normal

Thus, both statin treatment, via decreased coQ10, and thiamine deficiency, via reduced α-ketoglutarate dehydrogenase complex activity, can result in impairment of mitochondrial oxidative phosphorylation. It is possible that the lactic acidosis was the result of the combination of both thiamine deficiency and statin treatment, such that removal of one element was sufficient to resolve the metabolic stress and result in the resolution of acidosis.

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