Failure of Normal Glycaemic Regulation in a Patient With Severe Hypothermia

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Abstract
This report describes the case of an 88-year-old non-diabetic female who presented to the emergency department severely hypothermic following a presumed hypoglycaemic collapse due to self-neglect. Subsequent rewarming and resuscitation demonstrated a number of the significant consequences of severe hypothermia, including apparent secondary impairment of glycaemic autoregulation. The phenomenon of reversible inhibition of insulin secretion due to severe hypothermia has previously been documented in the field of cardiac surgery. The hyperglycaemia was not treated with any antihyperglycaemic agent, and her recovery was uneventful. Subsequent blood sugar level monitoring was normal. If administering insulin to the hypothermic patient, intensive monitoring of blood glucose is essential due to the increase in endogenous insulin secretion on rewarming.

Keywords
Hypothermia; Hyperglycaemia; Hypoglycaemia.

1. Introduction
Accidental hypothermia is a potentially life-threatening condition of particular concern during the winter months, although it may occur in any season. Hypothermia may be classified according to core body temperature as mild (35 to 32°C), moderate (32 to 30°C) or severe (less than 30°C) [1], and predisposing factors may include impairment of thermoregulation, a cold external environment, neglect (including self-neglect), hypothyroidism, and hypoglycaemia [1-3]. Systemic effects of hypothermia may include cardiac arrhythmias, loss of normal glycaemic control, and depressed level of consciousness [1,4-6]. The Advanced Life Support Course Provider Manual [1] offers guidance regarding many aspects of rewarming the hypothermic patient but does not specifically address glycaemic control. The case described here illustrates that significant derangements of blood sugar level may be encountered in severe hypothermia, even in the non-diabetic patient.

2. Case Report
An 88-year-old lady seemed confused and dysarthric when telephoned by her daughter. The daughter entered her home with police assistance, and found her lying on the floor partially clad and unable to communicate. Examination of the house showed that she had not been to bed the night before. She was last seen by her daughter twenty hours previously, at which time she had appeared fit and well. Her only pre-existing medical conditions were high blood pressure and treated hypothyroidism, though her appetite had been poor for some time. At the scene the paramedics found her blood sugar level (BSL) to be 1.2mmol l⁻¹ and administered intramuscular glucagon. On arrival in hospital it had risen to only 1.9mmol l⁻¹. Her Glasgow Coma Scale (GCS) score was noted to be 11 (Eyes 4 Verbal 2 Motor 5) and her temperature by tympanic thermometer was 27.8°C. She was maintaining her own airway, breathing spontaneously, and had an irregular femoral pulse of 60bpm. A brachial blood pressure reading could not be obtained. Secondary survey revealed only a minor skin tear to the left elbow. Pupils were noted to be unreactive but the daughter related a history of cataract surgery. Active rewarming was commenced. As the time of initial onset of hypothermia was unknown it was decided to rewarm at a rate of one degree per hour, giving a total rewarming time of ten hours. This was achieved by means of a warm air blanket and warmed intravenous fluids. She was catheterised to allow monitoring of urine output and offer the option of warm bladder lavage if her core temperature...
failed to rise. 50ml of 50% dextrose was administered intravenously for hypoglycaemia, resulting in a rapid increase in BSL to 20.4mmol L⁻¹. BSL then remained persistently elevated, falling gradually to 10.9mmol L⁻¹ at ten hours and 7.7mmol L⁻¹ after fourteen hours (see Figure 1). Arterial blood gases showed her to have severe metabolic acidosis due to lactic acidosis, with an uncorrected pH of 7.05, a pCO₂ of 2.4kPa, and a blood lactate of 15.0mmol/L (see Table 1). This is attributable to poor tissue perfusion resulting from her hypothermia. Her blood pressure became measurable after half an hour at 94/26 mmHg and after one hour, with a core temperature by tympanic probe of 28.7°C, her GCS had risen to 14 (Eyes 4 Verbal 4 Motor 6). She remained dysarthric and confused. Neurological examination at this time was otherwise normal. Cardiac monitoring showed initial slow atrial fibrillation (AF) interrupted by spells of ventricular fibrillation, however the latter were consistently of less than a second in duration and resolved spontaneously. Towards the end of the first hour these spells ceased and she remained in slow AF. She was then transferred to HDU for continued rewarming, and received a one-off 200mg bolus of intravenous hydrocortisone on suspicion of a possible autoimmune process targeting thyroid, pancreas and adrenal glands.

The following day she was both normothermic and consistently normoglycaemic, with a blood pressure of 147/66 mmHg, a pulse of 78bpm in sinus rhythm, and both the confusion and the dysarthria had resolved. She was therefore transferred to a medical ward. On examination she appeared neurologically intact. The remainder of her stay was uneventful and she was discharged home with a care package four weeks later. Outpatient clinic follow-up at 1 month post discharge revealed significant and symptomatic postural hypotension (BP 120/60 lying, 80/40 standing), which was successfully treated by adjusting her blood pressure medications. She continued fit and well at 4 months post discharge and no further hospital follow-up has been planned.

3. Discussion

It is hypothesised that this patient became hypoglycaemic as a result of poor appetite leading to prolonged self-neglect. This led to a depressed level of consciousness, and a combination of hypoglycaemia, exposure and possible hypothyroidism caused her to become hypothermic. Failure to respond to glucagon may have been caused by decreased muscular perfusion due to immobility and hypothermia, or it may have reflected low hepatic stores of glycogen resulting from both poor nutrition and overnight fast, or an altered metabolism secondary to hypothermia [4]. Her prolonged hyperglycaemia following a bolus of 50% dextrose is unlikely to be diabetic in origin given the negative history and subsequent normal glycaemic autoregulation. Steroids can affect glycaemic homeostasis but after administration of 50% dextrose there was an interval of over an hour before the patient received hydrocortisone, during which normal glycaemic autoregulation was conspicuously absent. It may be attributable in part to the slow absorption of glucagon from the injection site but at this stage little rewarming had actually taken place and we may assume that muscle perfusion remained poor. The most likely cause of the hyperglycaemia is the development of reversible suppression of insulin secretion as a result of hypothermia, as has previously been documented in patients undergoing hypothermic cardiac surgery [4-6]. If intravenous insulin is administered, pancreatic secretion of insulin on rewarming may be disproportionate to physiological requirements, carrying the risk of rebound hypoglycaemia [6-7]. Peripheral insulin resistance has also been noted during hypothermic cardiac surgery [4] but is attributable to anaesthesia and surgical stress. Whether hypothermia also causes peripheral insulin resistance, necessitating increased doses of exogenous insulin, is unclear. The key to good glucose control in the hypothermic patient is therefore intensive monitoring of blood glucose level, together with careful administration of an exogenous insulin infusion if indicated. Subsequent to this patient receiving hydrocortisone, disturbance of glycaemic autoregulation due to steroids may also have become significant. Once again, intensive monitoring, together with careful and appropriate use of exogenous insulin will provide optimal glucose control.

Many of the physiological disturbances arising from hypothermia resolve spontaneously as the core temperature rises. In this patient, cardiac arrhythmia, loss of glycaemic regulatory function, severe metabolic acidosis and neurological dysfunction all resolved through simple supportive measures and an appropriate programme of careful rewarming.

The patient did not receive exogenous insulin but a review of the literature suggests this may be beneficial. Good glycaemic control in surgical patients is associated with a reduced risk of post-operative infection [8] and a significant reduction in morbidity and mortality in the Intensive Care Unit [9]. In particular, significant reductions were demonstrated in rates of septicaemia and mortality.
due to septic foci, and also of acute renal failure and critical-illness polyneuropathy. Whether the benefit also extends to medical patients remains unproven but as intravenous insulin therapy is well tolerated, tight glycaemic control offers considerable potential benefits at relatively low risk.

4. Conclusion
Severe hypothermia may cause a reversible failure of insulin secretion and peripheral insulin resistance. In the hyperglycaemic hypothermic patient who is not a known diabetic, while tight blood glucose control may potentially confer a significant mortality benefit, the care team should be aware that the patient may exhibit rebound hypoglycaemia when secretion of endogenous insulin resumes, and intensive monitoring of blood glucose levels is therefore necessary. As the secretion of endogenous insulin may at first be excessive, intensive monitoring should continue even after return of spontaneous normoglycaemia.

5. Acknowledgements
The author thanks the patient for permission to publish.

6. Conflict of Interest Statement
None

Table 1
Arterial blood gas analysis report on admission

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<th>Parameter</th>
<th>Value</th>
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<td>Temperature (measured)</td>
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<tr>
<td>pH (measured)</td>
<td>7.16</td>
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<tr>
<td>pO(_2) (measured)</td>
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<td>pO(_2) (temperature corrected)</td>
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<td>pCO(_2) (measured)</td>
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<tr>
<td>pCO(_2) (temperature corrected)</td>
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<td>K(^+)</td>
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<tr>
<td>Ca(^{2+})</td>
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<tr>
<td>Corrected Ca(^{2+}) (pH 7.4)</td>
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<tr>
<td>Base Excess (blood)</td>
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<tr>
<td>Hb</td>
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<td>Haematocrit</td>
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</table>
7. References


Figure 1

![Graph showing blood sugar levels and temperature over time.][1]

- Blood Sugar Level (mmol/l) by BSL analyser
- Blood Sugar Level (mmol/l) by ABG analyser
- Temperature (°C)

5% Dextrose infusion commenced

Infusion to 0.9% NaCl

50% Dextrose bolus

Hydrocortisone administered

Time After Admission (hh:mm)