Addison's Disease: when is a "normal" random cortisol normal?

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A 38 years old man presented with eight months history of chronic abdominal pain of gradual onset associated with anorexia, fatigue and lethargy. He had lost 7 kg in weight. There were no other symptoms to suggest of gastrointestinal, neoplastic, connective tissue or infectious disease. On direct questioning he admitted that he had noticed increased skin pigmentation over the previous months in spite of consciously avoiding sun exposure.

Past history included a road traffic accident (RTA) two years previously resulting in head injury causing an extradural haematoma and contusion of his left kidney. The RTA had resulted in no long-term sequelae. Previously he had been investigated for weight loss and had several endoscopies which showed mild esophagitis due to gastro-oesophageal reflux.

On examination he was noted to be tanned. Blood pressure was 93/67mmHg with no postural drop. Pulse was 62bpm. There was no goitre. Examination was otherwise unremarkable.

Investigations included a normal glucose, full blood count, calcium and liver function test. Serum sodium and potassium were 136 and 4.1 mmol/l respectively. TSH was slightly elevated at 8.63 µIU/ml. Free T4 was 17.29 pmol/l. Thyroid peroxidase antibodies was elevated (>1000IU/mL). Random cortisol (afternoon sample) was 173 nmol/l. A short synacthen test was requested in view of clinical suspicion and showed serum cortisol of 195nmol/l and 182 nmol/l at 30 and 60 minutes respectively. Plasma ACTH was performed the next day and was raised at 159 (normal range 0-10.2) pmol/l confirming the diagnosis of primary adrenal insufficiency. The patient was commenced on hydrocortisone 10+ 10 + 5mg and fludrocortisone: 0.1mg daily.

A "normal" random cortisol in this case did not exclude diagnosis of adrenal insufficiency. This case highlights the importance of clinical judgement and raises the question of normality threshold for a random serum cortisol in the diagnosis of adrenal failure.