Introduction:
The hypothalamic-pituitary-adrenal (HPA) axis is a key regulator of critical illness. Cortisol and adrenocorticotropic hormone (ACTH) are pulsatile, which emerges from the feedforward - feedback of the two hormones[2]. Different genes are activated by continuous or pulsatile activation of the glucocorticoid receptor, even when the total amount is the same[1]. We aimed to characterise the ACTH and cortisol profiles of patients who were critically ill after cardiac surgery and assess the impact of inflammatory mediators on serum cortisol concentrations.

Methods:
20 patients with >2 organ system failure, >2 days after cardiac surgery were recruited. Total cortisol was assayed every 10 min, ACTH every hour and IL1, IL2, IL4, IL6, IL8, TNF-α every 4 hours. Cortisol binding globulin (CBG) was assayed at 0 and 24hrs. The relationship between cortisol and the inflammatory mediators was quantified in individual patients using a mixed regression model.

Results:
All profiles showed pulsatility of both cortisol and ACTH and there was concordance between the two hormones (See Fig 1). One patient died after 23 hours (see Fig 2). This patient lost pulsatility and concordance of cortisol and ACTH. Mean CBG was 26.89μg/ml at the start of sampling and 28.13μg/ml at the end. There was an association between IL6 (p=0.0002), IL10 (p<0.0001), IL4 (p=0.029) and serum cortisol levels. There was no association between the other mediators and cortisol.

Conclusion:
Cortisol and ACTH are both pulsatile in critical illness. Because pulsatility emerges from the interaction between the two hormones[2] – the premise of a ‘disconnect’ between the pituitary and adrenal gland is refuted. IL6, IL10 and IL4 may have roles in the control of cortisol during critical illness.

References:

Image 1:
[Image: Example of one patient undergoing 24 hour sampling of cortisol and ACTH (Patient survives).]

Image 2:
Fig 2. Example of one patient undergoing 24 hour sampling of ACTH and cortisol (Patient dies at hour 23).