alterations in ACTH precursors and key enzymes controlling ACTH maturation and secretion in a mouse model of sepsis-induced critical illness.

Methods
C57Bl/6 mice were randomly allocated to a healthy control group or to 4 critically ill groups sacrificed after increasing illness duration (30 hours, 3 days, 5 days, and 7 days). Critical illness was induced by sepsis brought about by cecal-ligation and puncture followed by fluid-resuscitation and antibiotics treatment. The study was continued until 15 surviving animals per time cohort were reached (n=120). We quantified pituitary pro-opiomelanocortin (POMC) gene/protein expression and POMC plasma concentrations, pituitary POMC intracellular trafficking and cleavage via intracellular POMC sorting/trafficking receptor Carboxypeptidase E (CPE) and prohormone convertase 1 (PC1/3) gene/protein expression. Gene expression of Annexin A1, an inhibitor of mature ACTH secretion, was quantified as marker of GR-mediated CORT-induced feedback inhibition at corticotroph level.

Results
Plasma CORT concentrations were median 3-fold increased during critical illness (p<0.001 for all time cohorts) in the face of normal (for 30H, 3D and 5D cohorts) to low (7D time cohort; p=0.01) plasma ACTH concentrations. Plasma POMC concentrations were higher in critically ill than in control mice (p<0.05). POMC gene expression (but not protein, p=0.8) was a median 55% higher in critically ill mice than in controls (p<0.05 for all time cohorts). In contrast, pituitary mature ACTH protein concentration was median 61% lower in critically ill than in control mice (p<0.001). CPE gene expression was only increased in 30H time cohort (p<0.001). PC1/3 gene and protein expression were positively correlated (R²=0.1; p=0.001) and were reduced (by 37% and 43%, respectively) during the entire course of critical illness (p<0.01). Annexin A1 gene expression was increased during critical illness (p<0.05 for all time cohorts).

Conclusion
Suppressed CRH or AVP signaling and GR-mediated action within corticotrophs explained lack of elevated plasma ACTH in critical illness, as indicated by impaired POMC processing and ACTH maturation. However, increased POMC gene expression suggests ongoing corticotroph activation, the driver of which needs to be identified.

1. Teblick A et al. Nat Rev Endocrinol 2019

Adrenal

**ADRENAL - TUMORS**

**Epidemiology of Adrenal Tumors: A Population Based Study of 1287 Patients**

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**SAT-176**

**Background:** Adrenal tumors are reported in 5% of adults, with malignancy rates in 1–12%, and rates of overt hormonal excess in 1–15%. However, most estimates originate from convenience samples. Our objective was to determine the incidence, prevalence and clinical presentation of adrenal tumors in a population-based setting.

**Methods:** We used a centralized epidemiologic database to identify patients diagnosed with adrenal tumors in a local community from 1995 to 2017. The database is a unique medical records linkage system that allows access to hospital and community medical records for local residents (population 137,000). We calculated incidence rates (IR) as the number of new patients diagnosed while living in the study area, and prevalence as the number of patients living in the study area on Dec 31 2017. IR and prevalence were sex- and age-adjusted to the 2010 US Census population.

**Results:** Of 1,287 patients diagnosed with adrenal tumor, the median age of diagnosis was 62 years (IQR 52–72), 713 (55%) were women, and 13 (1%) were younger than 18 years at diagnosis. IR was highest in patients >65 YO, followed by patients 40–64 YO, 18–39 YO and <18 YO (142 vs 66 vs 9 vs 2 per 100,000 persons years). IR per 100,000 increased from 4.4 (CI95% 0.3–8.6) in 1995 to 47.8 (CI95% 36.9–58.7) in 2017. Overall prevalence in the population was 0.53% in 2017, ranging from 0.01% among 0–17 YO to 1.9% among >65 YO.

Malignant adrenal mass was diagnosed in 8.7% patients (4 patients with adrenal cortical carcinoma (0.3%) and 108 (8.4%) patients with other malignant mass). Pheochromocytoma was diagnosed in 11 (1.1%) patients and benign adrenal mass was diagnosed in 1,175 (90.2%) patients (1,076 (83.6%) with adrenal adenoma and 85 (6.6%) with other benign mass). Median tumor size was 15 mm (range 5–255), and 184 (14%) of patients had bilateral tumors. Only 255 (20%) patients had dexamethasone suppression test, 93 (36%) with cortisol>1.8 mcg/dl. Of 1,076 adrenal adenomas, 53 (4.9%) had overt hormone excess, 140 (13%) had nonfunctioning adrenal adenomas, and 88 (8.2%) had mild autonomous cortisol secretion. Hormonal work up for was incomplete in 795 (73.9%) adenomas. Patients discovered incidentally (1,050, 81.6%) had a lower rate of malignancy and hormone excess (5.3% vs 52% of patients with non-incidental discovery, p<0.001).

Rate of malignancy was highest in children (67% vs 8% >18YO, p<0.001), bilateral tumors (16% vs 8% unilateral, p<0.001), tumors ≥4 cm (33% vs 7% in <4 cm, p<0.001).

**Conclusion:** IR of adrenal tumors increased 10-fold since 1995, and was highest in patients >65 YO. 8.7% of tumors were malignant, with a majority represented by malignant adrenal tumors other than adrenal cortical carcinoma. The risk of malignancy was highest in non-incidental discovery, children, and tumors > 4 cm. Overt hormone excess was diagnosed in 4.5% of patients. The majority of patients with adrenal adenomas had a suboptimal work up for hormone excess.

**Adrenal**

**ADRENAL - HYPERTENSION**

**Clinical Characterizations of Aldosterone- and Cortisol-Producing Adrenal Tumors in Primary Aldosteronism**

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Objective: Aldosterone- and cortisol-producing adrenal tumors (A/CPTs) are considered to be a subtype of primary aldosteronism (PA). The clinical characterizations of these tumors are still unclear, and they are often neglected by clinicians. The aim of this study was to summarize the clinical characterizations of these tumors to reduce the missed diagnosis.

Methods: The clinical, imaging and pathological data of patients with PA admitted to our hospital from January 1, 2013 to December 31, 2016 was reviewed. All the PA patients with a combination of a positive aldosterone-to-renin ratio (ARR) and a positive captopril challenge test (CCT), in whom the dexamethasone inhibition test was performed as well, were included in our study. These patients were divided into two groups, A/CPTs group and simple PA group, according to the function of cortisol secretion. The data of the two groups were compared and analyzed with SPSS 23.0. \( P < 0.05 \) was statistically significant.

Results: There were 87 patients with PA included in our study, 32 of whom (36.8%) were diagnosed with A/CPTs. In these 32 A/CPTs patients, 31 patients (96.9%) were combined with subclinical Cushing syndrome. Compared to these in simple PA group (n=55), the patients in A/CPTs group (n=32) were elder \( (53.81 \pm 10.70 \text{ ys} \ vs \ 48.42 \pm 10.17 \text{ ys}, \ P = 0.022) \), with larger diameter of adrenal tumors \( (1.50 \text{cm} vs 1.15 \text{cm}, \ P = 0.001) \), higher fasting plasma glucose \( (5.33 \text{mmol/L} \ vs \ 4.99 \text{mmol/L}, \ P = 0.047) \), higher serum cortisol levels and lower serum ACTH levels \( (\text{all } P < 0.05) \). 24 patients in A/CPTs group and 23 patients in simple PA group underwent adrenalectomy. 6 patients \( (25.0\%) \) in A/CPTs group and 3 patients \( (13.0\%) \) in simple PA group received glucocorticoid replacement therapy after adrenalectomy.

Conclusions: The prevalence of A/CPTs in PA is high. The patients with A/CPTs are mainly combined with subclinical Cushing syndrome, and prone to need glucocorticoid replacement therapy. Therefore, we recommend that all patients with PA should evaluate the function of cortisol secretion, and all patients with A/CPTs should be followed up closely after adrenalectomy to reduce the morbidity of adrenal insufficiency.

Diabetes Mellitus and Glucose Metabolism

**CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES**

**Chronic Unpredictable Environmental Stress May Induce Predisposition to Diabetes Mellitus**

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MON-648

**Title:** Chronic Unpredictable Environmental Stress may induce predisposition to diabetes mellitus

**Objective:** Chronic unpredictable environmental stress (CUES) may induce predisposition to diabetes mellitus.

**Material & Methods:** This study investigates the role of CUES on impaired homeostasis. Stressed group mice \( (n=20) \) were exposed to CUES for 16 weeks. Weekly body weight, feed consumption, feed efficiency ratio, fasting blood glucose were monitored. Plasma HbA1c, plasma cortisol, plasma epinephrine and plasma insulin, serum lipids, antioxidants and carbohydrate metabolizing enzymes activity were assessed along with DNA damage and histopathological examination of liver, kidney, pancreas, spleen and skeletal muscles. Semi-quantitative expression of IL-4, IL-6 and \( \beta \)-actin was also assessed.

**Results:** Fasting blood...