460.3166 and 474.2957 were detected, using MALDI, in renal sections, close to the predicted masses of 458.3013 (Δppm=0.65), 460.3169 (Δppm=0.65), and 474.2962 (Δppm=1.05), for derivatives of 11-dehydrocorticosterone, corticosterone and aldosterone respectively. Untargeted evaluation of ions was conducted to find regional markers that would allow definition of kidney histological zones. The Heat maps generated indicated that corticosterone intensity was higher in the inner cortex area close to the corticomedullary junction than the rest of the kidney. In contrast 11-dehydrocorticosterone was detected mainly in medulla and aldosterone signal was equally strong in medulla and outer cortex. Thus, MSI can be used map the sites where glucocorticoid and mineralocorticoids are most active in regulating renal tubular function. Co-localisation of steroids of interest with zonal markers by MSI permits steroid mapping in functional renal zones of the kidney. This approach provides fundamental new insights into the physiological control of sodium transport by steroids and opens doors to understanding changes in disorders of blood pressure. The project was supported and funded by Kidney Research UK.

Thyroid

FROM HYPO- TO HYPERTHYROIDISM

A Randomised, Controlled Trial of Adjunctive Cholestyramine or Prednisolone Compared to Standard Therapy for the Treatment of Uncontrolled Graves' Disease (the Chops Study)

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Introduction: Antithyroid drugs (ATDs) are recommended effective treatment for uncontrolled Graves' disease but achieves maximal antithyroid effects between 6 to 12 weeks. Cholestyramine sequesters thyroid hormones in the intestine and enhances its fecal excretion. Steroids inhibits the conversion of thyroxine to triiodothyronine peripherally and blocks thyroid hormone production. We hypothesize that adjunctive cholestyramine or prednisolone to ATDs may reduce circulating thyroid hormones and improve biochemical control.

Methods: In this multicenter, open labelled, parallel-group trial, we randomly assigned in a 1:1:1 ratio, adult Graves' disease patients with moderate to severe hyperthyroidism (FT4 levels > 40 pmol/L) to receive either adjunctive cholestyramine 4g twice daily or prednisolone 30 mg daily in tapering down doses in addition to standard treatment or standard treatment alone for 4 weeks. Standard treatment was carbimazole 30mg daily and propanolol 40mg BD for 4 weeks. The primary endpoint was change from baseline for FT4 and FT3 levels at the end of 2 and 4 weeks of intervention. Safety endpoints including gastrointestinal adverse events, hypokalemia, hypothyroid and hyperglycemia were recorded.

Results: A total of 107 patients were screened and 97 patients randomised. Baseline demographics, clinical and biochemical characteristics were similar between the groups. The baseline median FT4 levels were 51.6 pmol/L (42.2-71.1) and FT3 levels 22.5 pmol/L (5.7-30.8). Both FT4 and FT3 declined at two and four weeks from baseline but were no different between the three groups. At week 2, median FT4 levels declined by 43.3% (25.8-53.3), 39.8% (19.1-55.1) and 33.4% (20.1-62.0) (p=0.988) and at 4 weeks, 50.9% (33.3-63.8), 57.8% (39-70.9), 55.8% (36.2-72.0) (p =0.362) in the cholestyramine, prednisolone and standard treatment group respectively. Median FT3 levels reduced by 51.2% (22.8- 58.9), 59.9% (38.9-69.3) and 50.9% (26.9-63.9) (p=0.084) at week 2 and 60% (39.2-67.9), 67.5% (38.4-78.4), 63.1% (45.7-69.3) (p=0.387) in the corresponding cholestyramine, prednisolone and standard treatment only group. A higher number of gastrointestinal adverse events: constipation, bloating, diarrhea, abdominal pain and vomiting were observed in the cholestyramine group in the first 2 weeks of treatment and no difference in the incidence of hypokalemia between groups.

Conclusion: Adjunctive cholestyramine or prednisolone did not improve the biochemical control of uncontrolled moderate to severe Graves' disease when added to ATDs. The additional use of cholestyramine resulted in a higher number of gastrointestinal adverse events but were mild and self-limiting.

Thyroid

FROM HYPO- TO HYPERTHYROIDISM

A Tale of Two Therapies- A Comparison of Armour Thyroid and Levothyroxine

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Treatment of hypothyroidism is predominantly with levothyroxine due to its ability to generate stable T3 levels and its long half-life. Many patients report continued hypothyroid symptoms despite normal TSH values on levothyroxine and request to switch to desiccated animal thyroid extract. Desiccated thyroid extract is less used for fear of side effects and risks. There are only a handful of studies available comparing desiccated animal thyroid extract to levothyroxine. We conducted a retrospective study on 250 hypothyroid patients over the age of 18 who presented to our clinic from 2008-2018. We excluded patients who had a history of thyroid cancer and documented non-adherence. We analyzed 125 patients on levothyroxine (males=43, females=82) and 125 patients who were on levothyroxine but chose to switch to Armour Thyroid (males=7, females=118). We examined the following variables; when comparisons of proportions were made between the two groups, N-1 chi square test was used to determine significance.

1. Reason for change to Armour Thyroid from levothyroxine: Top reasons were fatigue (n=51/125, 40.8%), inability to

lose weight (n=32/125, 25.6%), mental fog (n=8/125, 6.4%), hair loss (n=8/125, 6.4%) and desire for a natural product (n=7/125, 5.6%)
2. Percentage of patients complaining of fatigue/weight gain in euthyroid state: 16/125 (12.8%) of patients on Armour Thyroid and 29/125 (23.2%) of patients on levothyroxine had complaints of fatigue and weight gain with a normal TSH. This 10.4% difference was significant (p value=0.033, 95% CI 0.84% to 19.8%).
3. Presence of side effects: 24/125 (19.2%) patients on Armour Thyroid discontinued it before 6 months. The top reasons were no improvement of symptoms (n=9/24, 37.5%), palpitations (n=5/24, 20.8%), worsening anxiety (n=3/24, 12.5%), cost (n=2/24, 8.33%), and loss of appetite (n=2/24, 8.33%). 5/125 (4.00%) patients on levothyroxine chose to discontinue it before 6 months. The reasons included presence of palpitations (n=3/5, 60.0%), hair loss (n=1/5, 20.0%), and gluten intolerance (n=1/5, 20.0%). A total of 11/125 (8.8%) had adverse effects from Armour Thyroid while 4/125 (3.2%) of patients on levothyroxine had adverse effects to the medication. The difference of 5.6% leaned toward clinical significance and trended toward being statistically significant (p value=0.06, CI -0.4842% to 12.1677%). Our research shows that patients generally feel better on Armour Thyroid compared to levothyroxine. Armour Thyroid is an effective medication to use for patients who remain symptomatic on levothyroxine and should be considered as a viable option in clinical practice. However, our study also indicated that patients may have more adverse effects on Armour Thyroid when compared to levothyroxine and further studies are needed comparing the two medications. Limitations of our study include the retrospective nature of the study and the sample size.

Thyroid

FROM HYPO- TO HYPERTHYROIDISM

Antiepileptic Drugs and Thyroid Hormone Homeostasis: Literature Review and Practical Guideline

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Thyroid hormones play an essential role in central nervous system development, normal physiological brain function and repairing mechanisms. On one hand, thyroid hormone alterations influence cortical excitability and on the other hand anti-epileptic drugs (AEDs) are associated with alterations in thyroid hormone metabolism. Although this interaction has long been described, and epilepsy is a common and chronic neurological disease, studies describing the interplay are often small and retrospective.
We performed a systematic review of the current literature on epilepsy, AED therapy and thyroid hormone metabolism. Forty-seven studies were included.
Most studies were retrospective cross-sectional studies (n=25) and investigated thyroid function alterations in patients on older AEDs such as phenobarbital, phenytoin, carbamazepine and valproic acid. Overall, almost one third of patients with epilepsy had subclinical hypothyroidism, especially patients on valproate and carbamazepine. Studies with patients receiving polytherapy are scarce, but reported a higher risk for hypothyroidism in patients with older age, female sex, longer duration of epilepsy, intractable epilepsy and polytherapy. Studies on newer AEDs are also scarce and further studies essential to improve the care for epilepsy patients.
AEDs are associated with alterations in thyroid hormone metabolism. Thyroid function monitoring is indicated in patients on AEDs, especially those with refractory chronic epilepsy and those on polytherapy. We provide a practical guideline for thyroid function monitoring for the clinician taking care of patients on AEDs.

Thyroid

FROM HYPO- TO HYPERTHYROIDISM

Association of Thyroid Function With Suicide Ideation/Attempt -A Systematic Review and Meta-analysis

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Background: Thyroid disorders are very prevalent and could affect virtually the entire human body, including cognitive and psychiatric domains. However, the relationship between thyroid dysfunction and suicide is still controversial. **Material and Methods:** A systematic review and meta-analysis was conducted to describe the association of thyroid function with suicide ideation/attempt in adults. A comprehensive search from databases' inception (MEDLINE, EMBASE, Cochrane, PsycINFO, PsycArticles, PSYNDEX and Scopus) to July 20, 2018 was conducted with no language restrictions. We included studies that reported mean values and standard deviation (SD) of thyroid hormone levels [Thyroid-stimulant hormone (TSH), free T4 (FT4), free T3 (FT3), total T4 (TT4), and total T3 (TT3)] in patients with suicide ideation/attempt compared with controls. Four reviewers worked independently and in duplicate for assessment of inclusion criteria, data extraction, and assessment of risk of bias. The mean value and SD of the thyroid function tests were used to calculate the mean difference for each subgroup. Random-effects models for meta-analyses were applied. **Results:** Overall, 2278 articles were identified, and 13 observational studies met the inclusion criteria. These studies involved 2651 participants, including 817 participants diagnosed with suicidal ideation/attempt. Group sizes of patients with suicide ideation/attempt ranged from 7 to 122 participants with mean age ranging from 23 to 49 years. Control group sizes ranged from 8 to 464 participants with mean age ranging from 24 to 50 years. Two studies included only women, two