Since the pioneering work of Nobel Laureates Hench and Kendall in the early 1950’s, we have recognised the potent anti-inflammatory effects of adrenal glucocorticoids. As a result 1% of the general population is now taking chronic corticosteroid therapy and this rises to 3% in the over 70’s. These data reflect oral therapy only where the mean equivalent dose of prednisolone was 6.9mg/day. Add to this patients treated with inhaled steroids, steroid creams, topical preparations such as eye drops, nasal sprays and systemic preparations (intramuscular, intra-articular) and it is easy to appreciate how common corticosteroid therapies are prescribed. In many cases these are life-saving and/or disease modifying (e.g. asthma, inflammatory bowel disease, vasculitis, polymyalgia rheumatica, dermatitis), but in other cases steroids are frequently used without a strong evidence base (e.g. COPD, rheumatoid arthritis) and for too long a duration. Many exogenous synthetic steroids are licensed for therapeutic use in the UK and show marked potency over and above endogenous cortisol (e.g. prednisolone x5, beta/dexamethasone x35).

The normal adrenal gland secretes about 10-15mg of cortisol/day. When given in high doses in excess of normal daily cortisol production equivalents and for duration in excess of one month, Cushingoid features frequently occur (e.g. weight gain, thin bruised skin, osteoporosis, diabetes, hypertension). Several studies have focussed on glucocorticoid induced osteoporosis with 50% of patients developing low bone mineral density when treated for >12 months. Prophylactic bisphosphonate therapy is now recommended as preventive therapy. Furthermore, several studies have now shown increased cardiovascular mortality (2-3 fold) in patients taking long term steroids. Iatrogenic Cushing’s syndrome is increasingly recognised as an unwanted side effect of the increased use of corticosteroid therapy. There is a balance between the beneficial effects of the anti-inflammatory actions of corticosteroids and their long term harm.

In addition there is the issue of steroid suppression. Exogenous steroids act via the glucocorticoid receptor to dampen the inflammatory process but also cause negative feedback at the level of the hypothalamus-pituitary to suppress endogenous cortisol secretion. Clinically this is of limited consequences whilst the patient continues to take exogenous steroid, since this will negate any deficiency in endogenous cortisol. However in patients withdrawing from steroids, or those taking potent inhaled steroids this can become an issue with “addisonian” features (tiredness, postural hypotension, hyponatraemia) complicating the underlying clinical picture. Indeed in a recent study we showed that 50% of patients with COPD/bronchiectasis treated with fluticasone inhalation had a deficient cortisol response to exogenous ACTH and that adrenal insufficiency contributed to their clinical features. Paradoxically, treating these patients with low doses of hydrocortisone whilst their own HPA axis recovers, may improve symptoms and prevent a stress-induced adrenal crisis.
Proposed projects will explore these issues in more detail. For example, students could undertake a literature review of the evidence base for the use of corticosteroids in inflammatory conditions, define the prevalence of steroid use in various populations/diseases, their benefits and side effects focusing on iatrogenic Cushing’s syndrome. Glucocorticoid-induced osteoporosis and the prescription of bisphosphonate therapy might be one particular area of interest. The issue of endogenous steroid suppression in patients taking topical steroids (inhalers, nasal drops, creams) could be directly explored with guidance issued on steroid replacement that may improve the management of these patients. Focussed research studies are possible on targeted populations; interrogation and exploration of UHBFT-based clinical databases in others. Overall, students will gain a greater insight into the secretion, action and beneficial/harmful effects of corticosteroids that will be of direct clinical relevance whatever specialty of Medicine they chose to pursue.