Letters to the Editor

OVERVIEW

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Cancer immunotherapy and the management of side effects

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Editor – We thank Mahalingam and Newsom-Davis[1] for their overview of immunotherapy side effects and in particular immunotherapy-related endocrinopathies. Immunotherapy has revolutionised the treatment of numerous malignancies in recent years. This paradigm shift poses a challenge to oncologists and general internal physicians who are exposed to a range of immunotherapy-related endocrinopathies which may be outside their usual area of expertise. It is important that clinicians acquire the knowledge and skills necessary to manage to these side effects appropriately.

Mahalingam and Newsom-Davis' review[1] discusses the management of immunotherapy-related hypothyroidism. It is essential that clinicians must first differentiate primary hypothyroidism (due to thyroiditis) from secondary hypothyroidism (due to hypophysitis), which is defined as a low or inappropriately normal thyroid stimulating hormone (TSH) in the setting of a low free T4. Although thyroxine replacement is the appropriate treatment for primary hypothyroidism it risks precipitating an adrenal crisis in those with immunotherapy-related hypophysitis.[2] ACTH deficiency is the most commonly affected pituitary hormone deficit followed by TSH, with deficiency rates of 91% and 84% respectively in those receiving anti-CTLA-4 treatment.[3] Therefore, the presence of secondary hypothyroidism should raise immediate concern for adrenal insufficiency. Administration of thyroxine in this circumstance can precipitate an adrenal crisis as thyroxine increases the metabolism of (already deficient) cortisol.[4] An urgent assessment of the hypothalamic-pituitary-adrenal (HPA) axis with measurement of ACTH and cortisol is mandatory in patients presenting with secondary hypothyroidism. Once confirmed, hydrocortisone replacement should be initiated followed by thyroxine replacement at least 48 hours after.[2] In acutely unwell patients, hydrocortisone should be administered empirically prior to an assessment of the HPA axis.

It is also important for general physicians to note that thyroxine should be titrated to maintain a fT4 level in the upper half of the normal range. TSH cannot be used to titrate thyroxine in this setting as it will invariably be low. Although this may seem obvious, we frequently encounter patients with secondary hypothyroidism whose dose of thyroxine has been reduced as a low TSH is misinterpreted as thyroxine overreplacement rather than secondary hypothyroidism. We hope this letter will contribute to the improved understanding around the management of immunotherapy-related hypothyroidism. ■

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Where now for infection services in the NHS? What about children?

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Editor – We agree with Llewelyn *et al* that a fundamental review of NHS infection service provision is required.[1] However, we would suggest that this review should also include children's infection linked with the adult services they describe.

Llewelyn *et al* advocate 'removing barriers to training and service delivery' and 'training encompassing all aspects of infection service provision'. We would support these suggestions but feel they should be expanded to included paediatric infection.

Children's infection services have repeatedly been left out of recent attempts to improve infection services in the UK, despite a formal NHS England specialist service specification.[2] The best practice standards for the delivery of NHS infection services specifically excludes paediatric infection services, as these were felt to be 'outwith the scope of this document'.[3] Training in microbiology is not accessible for those with paediatric experience, only those who have undertaken training in adult internal medicine.[4] The majority of infection diagnostic laboratories will process samples for a paediatric population, but experience in Paediatric infection for those running these laboratories is becoming increasingly limited.

Children can be more affected by certain infections than adults (eg scarlet fever, respiratory syncytial virus), but may be the source of these infection to vulnerable adults. Conversely children can be affected by chronic infections in adult family members such as TB, HIV and hepatitis B and C. Managing all family members with the infection in a joined-up way is thus required.