Invitation to participate in a new UK Collaborative Network research project: Primary Hyperparathyroidism in Children.

Dear Colleagues

Primary Hyperparathyroidism in children is rare, and in comparison, with adults (prevalence 2–5 in 100,000 and 1–4 in 1,000 respectively), PHPT in children is about 100 times less common. It is, therefore, not surprising that our understanding of these children's presentation, diagnosis, and outcomes is limited. Another gap in our knowledge is genetic background of this condition. Although some germline mutations associated with PHPT (e.g. *MEN1, RET, CDC73, CDKN1B, CASR*) are well characterized, somatic genetic drivers of parathyroid adenoma (PA), parathyroid carcinoma (PC) and hyperplasia in children are largely unknown, in contrast to adults in whom *MEN1* and *CDC73* mutations are major drivers for PAs and PCs, respectively.

We would like to initiate a UK wide research project which will address these two important questions and will consist of two parallel studies:

1. **Diagnosis, treatment and outcomes of surgery in children with Primary Hyperparathyroidism in UK between 2000 and 2021.**
   This is a retrospective review of clinical presentation, diagnostic and therapeutic pathways and outcomes of surgery in children (<18 years) diagnosed with sporadic or familial PHPT in UK between 2000 and 2021. This study has been approved by our Joint Research Office at UCL as an Audit Project and collection of data on children treated in our centre has already started. We will ask collaborating centres to register this project with local R&D *(happy to share our application)* and to send us deidentified data on their young patients in a pre-determined format, which we will share with you once you join the study.
2. **UK wide genetic study of Primary Hyperparathyroidism in children; the somatic genetic drivers of PAs, PCs and hyperplasia.**
   This prospective study of somatic genetic drivers of PAs, PCs and hyperplasia in children with PHPT has also already started at our centres. Our hypothesis is that somatic genetic drivers of PHPT in children are different to adults and that somatic mutations might explain the phenotypic variability of inherited endocrine tumour syndromes. To define somatic mutations and their effect on the development of sporadic PAs, PCs and hyperplasia as well as their possible impact on phenotype variability in familial PHPT, we propose to extract RNA and DNA for WGS from fresh frozen parathyroid tissue (dry ice, liquid nitrogen) collected during surgery and perform germline DNA analysis from a child and both parents. Multicentre Ethics approval has been obtained (Genetics of Endocrine tumours, MRES number 06/Q0104/133, UKCR number 4663, IRAS number 33446) and once the clinician at a collaborating site approaches a family about participation, the coordinating centre will contact them to initiate the online consent process. We will also cover costs of transport of samples to London where they will be safely stored until analysis is done.

If you are interested in contributing to these studies, please contact Tom Kurzawinski (tom.kurzawinski@nhs.net), Philippa Prentice (philippa.prentice1@nhs.net) or Alexander Chesover (alexander.chesover@nhs.net) for further information.

We are looking forward to hearing from you

Best wishes,

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