They were type II meningeal cysts with necks connecting cyst bodies to the meningeal ostia. The dorsal roots of the spinal nerves were centred at the meningeal ostia, and then splayed over the cyst bodies or traversed the cyst cavities. The cyst necks pressed against the inferior border of the vertebral pedicle as they sharply turned inferolaterally into the intervertebral foramina, where the cyst bodies were halted laterally by the spinal ganglia.

This study, for the first time, reports the in situ macro/microscopic configuration of Type II cysts and their relationship with the thecal sac, spinal nerve roots and ganglia, vertebral pedicles and intervertebral foramina. These findings suggest a neck-linked valvular mechanism and indicate the necessity of localizing and ligating the cyst neck for surgical management of symptomatic Type II cysts.

Exploring the influence of patient covariates on the dose-response of vitamin D supplementation in pregnant women and their infants.

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Vitamin D deficiency during pregnancy is associated with an increased risk of pre-eclampsia and gestational diabetes in the mother and an increased risk of rickets in the infant. Supplementation of vitamin D during pregnancy is advocated but the recommended doses of existing regimens vary four-fold and are not individualised. This can potentially result in treatment failure or hypervitaminosis D. Therefore, this study aimed to explore the influence of patient covariates (e.g. age, sex, size, season, and ethnicity) on the dose-response of vitamin D supplementation.

Data were obtained from a published clinical trial of pregnant women (n = 260) and their infants (n = 260). Mother-infant pairs were randomised to either placebo (0 IU, 0 IU), low-dose (1000 IU, 400 IU), or high-dose (2000 IU, 800 IU) oral vitamin D3. Serum concentrations of 25-hydroxyvitamin D were obtained from mothers in two occasions and from infants in five occasions. Several pharmacokinetic (PK) models were fitted to the concentration data using nonlinear mixed effects modelling. The influence of covariates was explored using plots of posthoc estimates of the parameters versus the covariates and covariate modelling. Selection of the best model was evaluated using the likelihood ratio test and goodness-of-fit plots.

PK models for vitamin D supplementation in pregnant women and their infants were developed. A one-compartment model with first-order elimination was found to provide the best fit for both the pregnant women's data and the infants' data. No covariates were found to have a significant effect on the PK parameters of either model.

It is uncertain whether this lack of covariate effect on the disposition of vitamin D...
is real or whether the design (models and data) was inadequate to detect any covariate effect. However, based on this study, there is no evidence to support dose-individualisation of vitamin D3 based on the covariates tested here.

Ablation of hypothalamic RF-amide related peptide neurons with diphtheria toxin: effects on anxiety behaviours and reproductive hormone secretion.

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RF-amide related peptide (RFRP) 3 is a neuropeptide that inhibits central regulation of fertility. RFRP-3 infusions stimulate stress hormone secretion and anxiety-related behaviours. It is unknown if these findings reflect endogenous RFRP-3 fluctuations. This study aims to demonstrate a role for endogenous RFRP-3 in such responses by characterising the resulting behavioural phenotype in RFRP ablated mice using a novel transgenic technique to specifically ablate RFRP neurons.

A new transgenic mouse line in which the Rfrp gene also produces Cre recombinase was crossed with a line that enables Cre-dependant expression of the diphtheria toxin receptor. Consequently, injecting the offspring with diphtheria toxin resulted in apoptosis of cells expressing Rfrp.

RFRP neuron ablated female mice were compared against non-Cre expressing controls (n = 10/group) for anxiety behaviour (elevated plus maze (EPM) and light/dark box tests), obsessive-compulsive behaviour (marble-burying test), depression (forced swim test) and stress axis activity (acute restraint) 4 weeks post-diphtheria toxin treatment. Additionally, the effect of RFRRP ablation on the secretion of the reproductive gonadotrophic hormone luteinizing hormone (LH) was measured.

RFRP ablation had no effect on time spent in aversive areas of the EPM (P = 0.43, Mann Whitney-U test) and light/dark box (P = 0.13), marble-burying (P = 0.97) and active swimming duration (P = 0.48). Restraint caused an increase in circulating stress hormone (corticosterone) in both groups (basal: 47.5 ± 39.0, restrained: 214.0 ± 111.1 ng/mL, P < 0.05 two-way ANOVA) however the response did not differ between groups. In contrast, circulating LH concentrations were elevated in ablated mice compared to controls (0.79 ± 0.27 vs. 0.51 ± 0.24 ng/mL respectively, P < 0.05; unpaired t-test), and the suppressive effect of acute restraint stress on LH in controls (0.45 ± 0.19, P < 0.001 vs. basal levels; unpaired t-test) was not seen in ablated mice.

These data show that RFRP neurons suppress LH secretion and mediate stress induced LH suppression. They were not required for behavioural or stress steroid responses modelled here, although may still be involved in chronic affective disorders.

The overlap of hyperventilation syndrome with asthma and anxiety.

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Hyperventilation Syndrome (HVS) is a functional breathing disorder that causes recurrent or chronic respiratory and non-respiratory symptoms which cannot be attributed to a specific medical diagnosis. It is thought to be common yet often unrecognised or misdiagnosed as asthma. Asthma and HVS can co-exist and there are also similarities between HVS and anxiety disorders leading to diagnostic uncertainty. HVS is usually diagnosed by the Nijmegen questionnaire (NQ), a self-administered 16-item checklist for HVS symptoms. However, the NQ includes several symptoms that are also associated with asthma and anxiety disorders. The aim was to examine the poorly understood overlap of HVS with asthma and anxiety in a general population sample.

The prevalence of HVS and its association with various asthma measures and anxiety diagnosis at age 38 years were explored in the Dunedin Multidisciplinary Health and Development Study (‘Dunedin Study’). According to NQ in the Dunedin Study, HVS was more common in women (12.1%) than men (6.5%, P = 0.003). There was substantial overlap between HVS and asthma, with up to one-third of female asthmatics (35.4%) reporting symptoms suggestive of HVS. However, there were different patterns of symptoms in the NQ found between people in HVS-only and asthma-only groups. Conversely, there were no significant difference in asthma measures including lung function (FEV1/FVC ratio), bronchodilator responsiveness, and developmental asthma phenotypes between those with asthma only and those with both asthma and HVS. Further, approximately half of the HVS-only group were also diagnosed with anxiety, especially panic disorder. However, there remained a group of people whose high NQ score could not be explained by co-morbid anxiety diagnosis.

Taken together, HVS is a distinguishable clinical entity using the NQ that is common in the general population of young adults, and unlikely to be merely undiagnosed asthma or panic disorder.

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Energy expenditure associated with prolonged sitting, regular activity breaks, and physical activity

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Leptin receptor signalling in Agouti-related peptide (AgRP) neurons modulates puberty.

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The adipose-derived hormone leptin is required to communicate metabolic information to hypothalamic gonadotropin-releasing hormone (GnRH) neurons, the central drivers of reproduction. Metabolic signals provided by leptin are integrated with the reproductive system so that fertility can be closely linked with metabolic status. GnRH neurons do not possess leptin receptors (LepR), indicating that leptin acts through intermediate leptin-responsive neurons to exert effects. Neurons which are critical for leptin-to-GnRH signalling are GABAergic, which narrows the pool of candidate populations involved in this transfer of information. Agouti-related-peptide (AgRP) neurons in the arcuate nucleus of the hypothalamus are an attractive candidate population as they are GABAergic and possess LepR. This study aimed to investigate whether leptin actions on AgRP neurons are required for normal fertility.

Transgenic mice were generated using Cre-Lox technology where targeted expression of the Cre recombinase enzyme allowed specific removal of LepR from AgRP neurons. Puberty onset and fecundity of AgRP-LepR-knockout mice (n = 9) and female (n = 10) mice were compared to that of male (n = 10) and female (n = 10) control littermates. AgRP-LepR-knockout female mice exhibited a significant delay in the onset of reproductive cycles, which began on day 37.5 ± 1.0 compared to day 34.1 ± 0.85 in controls (P < 0.05, Mann-Whitney U test), however no deficits were observed in adult fecundity. No significant differences in puberty onset or fecundity were observed between male control and AgRP-LepR-knockout mice (P > 0.05, Mann-Whitney U test).

This study provides evidence that leptin signalling in AgRP neurons is involved in the development of reproductive function in female mice but is not required for adult fertility. A follow-up experiment using LepR-null mice in which the receptor is ‘rescued’ only in AgRP neurons to determine whether leptin signalling in this neuronal population is sufficient for fertility is currently underway.

Does Denonvilliers’ fascia exist in the female?

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Of all cancer deaths in New Zealand, 15% are attributed to colorectal cancer. Treatment may involve excision of the rectum and surrounding tissues. The prerectal surgical plane is demarcated by Denonvilliers’ fascia (DVF). Recognition of DVF is important to define the extent of direct rectal cancer spread when interpreting preoperative imaging. DVF was first described in the male as a “Distinct membranous layer”, giving no account to presence in the female thus existence of this structure in the female is controversial. This study aimed to map the configuration of DVF in adult female cadavers. Three sets of serial sections (two transverse and one sagittal) were collected from three adult female cadavers. Two sets were collected individually from two cadavers and plastinated using novel Epoxy-12 plastination technology, and examined under a dissection microscope.

The upper border of the external anal sphincter was
found to be a crucial landmark in the pre-rectal surgical plane. The area superior to the border was filled with adipose tissue. Inferiorly, the fibres of the rectal and vaginal walls intermingled and no fascial septum was identifiable. Fragmented membrane-like structures in the plane included (1) the peritoneal extension on the posterior vaginal fornix, (2) vascular fascial sheets and (3) tendinous fibres of the longitudinal rectal muscles.

These results indicate that there was no evidence of DVF in the female. Surgeons may misidentify the fragmented membrane-like structures as DVF.

Mapping perspectives on an ethically challenging paediatric case

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Neonatal care of infants with life limiting conditions provides ethical challenges for all involved including their whānau. Care of these infants often involves a large multi-disciplinary team (MDT), with each individual of this team bringing different perspectives and views to the care of these infants. Previous research in the field of paediatric bioethics tends to be theoretical and focus on “grey-zones” in decision making, particularly concerning when and if a parent’s decision can be overidden. However, little is known about how a multidisciplinary team actually navigates complex ethical decisions in the clinical setting, in affiliation with the family. This study aims to contribute to this gap in the literature.

This project was designed around a single ethically challenging neonatal case and employed qualitative interviews with both the family and a range of health professionals to explore the personal perspectives regarding ethical issues navigated through this single case.

Data was collected in the form of semi-structured, qualitative interviews and then analysed using grounded theory-lite methodology. One interview was conducted with the family, and seven interviews with members of the MDT (neonatologist, paediatrician, charge nurse, transport nurse, midwife, clinical geneticist and social worker).

A key theme from the data was the importance of communication in ethically complex cases. This theme arose from subthemes extracted from the interview data, including: 1) the role of information; 2) processes and procedures and 3) building a relationship. Subtle differences in the way in that different team members talked about these three sub-themes are described and interpreted.

Developing a nuanced understanding of the ethical aspects of such cases, from a multidisciplinary perspective, may help to optimise clinical care and could contribute to the development of inter-disciplinary education resources for health professionals.