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Vitamin D status of psychiatric inpatients in New Zealand's Waikato region

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Vitamin D deficiency is widespread in New Zealand and may be particularly common among people with a psychiatric illness. We studied 25-hydroxy vitamin D3 levels in an unselected sample of adult psychiatric inpatients in Hamilton (latitude 36.5 S) during the late winter when levels are near their nadir. Of 102 consenting subjects, 74 (73%) had vitamin D levels <50 nM and thus had at least mild deficiency, while 19 (19%) were moderately to severely deficient with levels <25 nM. Rates of deficiency were comparable for men and women; only the former showed a correlation of vitamin D levels with age ($r = 0.45$, $p<0.01$). Maori participants constituted half the sample (n=51) and were more likely to be deficient than their European counterparts ($p=0.04$). Vitamin D also varied by diagnosis, with schizophrenia associated with markedly lower levels than mania and depression ($p<0.001$). These findings support proposals to provide vitamin D supplementation to NZ psychiatric patients, particularly during the winter months.

Thyroid cancer and graves' disease: is surgery the best treatment option?

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Introduction: Graves' disease is a common cause of thyrotoxicosis. Treatment options include anti-thyroid medications or definitive therapy: either surgical removal of the thyroid gland or radioactive iodine (I^{131}) therapy. Traditionally, I^{131} has been the preferred definitive treatment for Graves' disease in New Zealand. Reports of concomitant thyroid cancer occurring in up to 17% of Graves' patients suggest surgery, if performed with low morbidity, may be the preferred option.

Aims: The aim of this study was to determine the rate of thyroid cancer and surgical outcomes in a New Zealand cohort of patients undergoing surgical treatment for Graves' disease.

Method: Retrospective review of patients in Waikato undergoing thyroid surgery for Graves' disease during the 10 year period prior to 1 December 2011 to assess the

incidence of associated thyroid cancer and surgical complication rates compared to patients with toxic multinodular goitre.

Results: A total of 833 patients underwent thyroid surgery. Of these 117 were for Graves' disease. The median age of the Graves' patients was 42 years. Total thyroidectomy was performed in 82, near-total in 33 and subtotal in 2 patients. Recurrent thyrotoxicosis developed in one subtotal patient requiring I^{131} therapy. There were two cases of permanent hypoparathyroidism (post total thyroidectomy) and one of permanent recurrent laryngeal nerve palsy (post near-total thyroidectomy). Eight patients (6.8%) had thyroid cancer detected, none of whom had overt nodal disease.

Five were papillary microcarcinomas (one multifocal), two were papillary carcinomas (11mm and 15mm) and one was a minimally invasive follicular carcinoma. During the same time period 34 patients underwent surgery (total thyroidectomy in 27 and near-total thyroidectomy in 7 patients) for a toxic multinodular goitre. Three cancers were identified all of which were papillary thyroid cancers (ranging from 0.5 to 10mm in size). No complications occurred in this group.

Conclusions: A low rate of incidental thyroid cancer was identified as compared to some previous reports. This may be influenced by how carefully the pathologist reviews the specimen. A low complication rate (<2%) of permanent hypoparathyroidism and nerve injury (<1%) supports surgery being a safe alternative to I^{131} especially for patients with young children, ophthalmopathy, compressive symptoms and those desiring pregnancy.

The effects of neonatal hypoglycaemia on vision and visual development at the age of two-years

Tzu-Ying (Sandy) Yu on behalf of the CHYLD Study team

Background: Neonatal hypoglycaemia is a perinatal adversity encountered by many newborns. When severe, this condition is known to have detrimental effects on neurodevelopment including vision. However, little is known about how the severity of hypoglycaemia can affect visual development and visual motion processing. The CHYLD (Children with Hypoglycaemia and their Later Development) group is a multi-disciplinary team investigating the neuropsychological development of young children who were at risk of developing neonatal hypoglycaemia. Currently, a follow-up study is being carried out on a cohort of children who as newborns were part of the BABIES and Sugar Babies studies conducted at Waikato Women's Hospital. As part of these previous studies, participants had continuous blood glucose monitoring from the time of birth until two to seven days of age.

Aim: To investigate the effects of neonatal hypoglycemia on visual function and cortical motion processing at the age of two-years.

Methods: Visual function assessments are performed using age-appropriate optometry tests within a 1 month window around two years' corrected age. Cortical motion coherence thresholds are measured with a psychophysics programme using a random dot kinetogram (RDK) stimulus. The two methods used to detect whether the

motion is visible are (i) objective measurements derived from observations of optokinetic reflex (OKR), and (ii) subjective measurements from the behavioural responses of the child (where possible).

Results: To date 250 study participants have been assessed. The mean of the motion coherence thresholds measured by OKR in this cohort of children is approximately four times poorer than normal values expected in adults. Preliminary results have also shown that although the majority of standard optometry tests do not correlate with our measure of cortical processing, there is an association between motion coherence thresholds and stereoacuity. Any relationship between neonatal hypoglycaemia and visual development is yet to be determined.

This analysis will be possible in approximately 12 months when all participants entering this study have been assessed and the investigators are un-blinded from blood glucose measurements.

Conclusion: Motion coherence psychophysics and clinical optometry tests can be applied to two-year-olds as a potential method of assessing cortical visual development.

Immune defence proteins in human milk: differences between pre-term and term deliveries.

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Besides providing a balanced source of nutrition, milk also contains a range of proteins that contribute to the defence against pathogens. These include immunoglobulins, as well as a range of less well characterised innate immune-related proteins. When ingested by the newborn, these proteins may contribute to maintaining a healthy digestive system for the baby by facilitating a normal repertoire of commensal bacteria and suppressing pathogenic bacteria.

The levels of some of these proteins have not been very well characterised in human milk. In particular, the extent to which they may be altered in milk from mothers that have had a shortened gestation period, for which the volume of milk supplied to the premature infant as well as its host defence requirements, may be significantly different compared with full term infants. We therefore obtained a preliminary estimate of the mean concentration in milk and the degree of variability in a population, of five innate immune proteins: IgA, lactoferrin, IgG, secretory component (SC), and the complement protein C3 as well as total protein.

Milk samples were obtained from 30 mothers having had either a normal gestation length (>36 weeks, n=10; T), a premature baby (between 33 and 36 weeks, n=10; P), or a very premature baby (between 28 and 32 weeks, n=10; V). Milk samples were

collected from each volunteer at approximately 2 weeks and 5 weeks after giving birth. The data were analysed by REML. Significant variability was observed over time within individual mothers, with coefficients of variation (CV) of 28%, 21%, 22%, 15% and 32% for IgA, lactoferrin, IgG, SC and C3, respectively. For IgA and C3, this was substantially higher than the technical variability of the assays, for which the CV ranged from 10-15%. A significant decrease from week 2 to 5 was observed within the T and P groups for all five proteins except IgG, but over this time the V group remained unchanged. The variability between individuals was substantially higher than that within an individual, with CVs ranging from 26 to 52%. While there were significant differences between the T, P and V groups for some of the comparisons, this was not consistent across all the proteins and time points. The total protein concentration decreased from week 2 to 5 in the P group but no changes over time were observed in the V and T groups. Comparing the total protein concentration among the groups, the only significant difference was that the T and P groups were higher than the V group at week 2.

It is conceivable that some of the observed variability is due to differences in milk volume. In summary, these results show there is considerable biological variability in the concentrations of these host defence associated proteins among individuals and that gestation length by itself appears to have no substantial effect on milk composition.

Cortisol suppression after a single dose of dexamethasone at surgical induction

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Purpose: The synthetic glucocorticoid dexamethasone is routinely used in patients receiving a general anaesthetic to reduce the risk of nausea, vomiting and the postoperative inflammatory response. Dexamethasone is known to suppress the hypothalamic-pituitary-adrenal axis however the duration of this suppression with the standard dose of 4-8mg used in anaesthesia is unknown.

Methodology: A randomised controlled double-blind crossover trial assessing the effects of intravenous 8mg dexamethasone versus saline control was performed using 10 healthy male volunteers. The cortisol and ACTH response was assessed over the next 5 days.

Results: Baseline testing demonstrated normal hypothalamic-pituitary-adrenal axis function in all individuals. No significant differences in cortisol levels as compared to placebo were demonstrated at either four hours or eight hours after dexamethasone administration however by 24 hours the cortisol had dropped to <5% of baseline and a significant difference in cortisol levels was demonstrated until day four post dexamethasone administration.

Conclusions: At the dexamethasone dose commonly used at induction significant suppression of the hypothalamic pituitary adrenal axis occurs. Whilst this suppression is maximal 24 hours post administration, the serum cortisol may not return to normal until the 4th day after dexamethasone administration. This may result in a risk of being misdiagnosed with adrenal insufficiency based on low cortisol levels over this time period.

Narrowband UVB phototherapy induces change in melanocytic naevi

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Introduction: Exposure to narrowband ultraviolet B (NBUVB) is known to induce morphological changes in melanocytic naevi but there have been few systematic studies of this process.

Method: Macro and dermoscopic images of prominent melanocytic naevi found in 51 subjects were taken immediately prior to a course of NBUVB; after 10 exposures; after 30 exposures or at the end of the treatment course if earlier; and 3 months after discontinuing treatment. Four dermatologists reviewed the images and agreed on the specific clinical and dermoscopic features of the naevi by consensus.

Preliminary Results: 36 of 51 patients had complete sets of images of a total of 440 naevi. The most common global dermoscopic patterns were reticular in 50%, and globular in 32%.

Following NBUVB exposure, 50% (218/440) of naevi underwent changes in local features ($p<0.001$). Blurring or merging of lines was noted in reticular naevi, whereas increased colour intensity and increased number of dots/globules were observed in globular naevi. Changes in local features were more readily observed in lighter skinned subjects ($p=0.05$). 40% of naevi (167/419) underwent change in size following UV exposure; of these, 54% 91/167) decreased in size, whilst 46% (76/167) increased in size. The trend was for these naevi to return to their pre-treatment size after phototherapy.

No changes suspicious of malignancy were observed in any lesions.

Conclusion: Around half of exposed naevi undergo changes following a course of NBUVB. Size tended to revert to pre-treatment values 3 months after discontinuing phototherapy.

Son of Doctor Strangelove: how we learned to stop worrying and love PHARMAC (New Zealand consumers' perceptions of private insurance for pharmaceuticals)

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Introduction: New Zealand's pharmaceutical strategy depends heavily on PHARMAC's effectiveness. PHARMAC has been praised for increasing access to pharmaceuticals while containing costs [1]. However, PHARMAC has also been criticised for denying patients timely access to expensive but potentially life-saving pharmaceuticals [2]. New Zealand's access to high cost medicines has been shown to lag behind comparable countries [3]. In light of this controversy, we aim to explore consumers' experience of public coverage, and willingness to pay for alternative coverage through private insurance.

Methods: Thirty pharmacies in the greater Auckland region were randomly selected from a list provided by the Pharmaceutical Society. An investigator approached every second customer over 5 days. Customers were asked to fill out an 18 question self administered questionnaire.

The questionnaire had been developed for this study and validated by two rounds of pilot tested. The study was approved by the University of Auckland Human Participants Ethics Committee.

Results: 46% of the 433 respondents had private insurance, but only 19% had coverage for pharmaceuticals. 52% were willing pay extra for pharmaceutical coverage. Of these, 67% were only willing to pay $20 per year, and only 7% were willing to pay $40 or more. Willingness to pay (or lack thereof) wasn't affected by age, gender, ethnicity, household income, level of education, frequency of pharmacy visits or pharmacy spending.

80% of respondents had experienced no problems with the public funding of their pharmaceuticals in the previous 12 months, 8% had problems with funding changes, 6% had problems with availability, and 5% with affordability. 67% were confident or very confident in the public system, with 15% not being confident and the remainder neutral.

Conclusion: Consumers show low willingness to pay for private insurance coverage of pharmaceuticals, and the majority have confidence in the public system.

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Prostate-specific antigen (PSA) testing in Waikato general practices

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Objectives: To examine patterns of PSA testing and its outcomes in twelve general practices in the Waikato region.

Methods: The study population included 11,346 men aged 40+ years enrolled in 12 Waikato general practices, who had a PSA test in 2010. All PSA results for 2007-2010 were obtained from the community laboratory with permission from the individual practices. Each practice provided baseline data of men aged 40+ years, including National Health Index number (NHI), date of birth and ethnicity. The practice records of men with elevated PSA test were searched for information on the reasons for testing and its outcomes, including biopsy and diagnosis of prostate cancer. Patterns of PSA testing were analysed by age and ethnicity.

Results: In total, 2,878 men aged 40+years (25.4 %) had a PSA test in 2010; ranging from 12.1% to 36.7% for the 12 general practices in the Waikato region. The testing rate for Māori men was 12.9% compared with 27.7% for non-Māori men. Three hundred and eighteen men (11%) had an elevated PSA, but only 56 (17.6%) of these could be considered as being asymptomatic screened patients. Out of the 318 men 78 had a biopsy (24.5%), and 41 were diagnosed with prostate cancer. The cancer per elevated PSA test rate was 13% in total; 6.7% for men aged 40-49 years, 10.7% for 50-59 year old men, 18.2% for 60-69 year old men, 14.9% for 70-79 year old men, and 4.1% for men aged 80+ years.

Conclusions: Significant disparities were observed in PSA testing between Māori and non-Māori men. Other factors, such as patient's age and practice policy seem to influence the testing rate. Further research will be conducted in the Midland region to explore the patterns and outcomes of PSA testing with regard to age, ethnicity, and rural/urban residence.

Myostatin splice variant in humans – does it exist?

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Introduction: Myostatin is an inhibitor of skeletal muscle myogenesis and antagonism of this protein provides potential for increasing muscle regeneration and growth.

A myostatin splice variant (MSV) is present in the Certartiodactyla clade of mammals due to a cryptic intron site in exon 3 of the myostatin gene. MSV acts as an endogenous antagonist of myostatin by binding directly to myostatin and the activin IIB receptor. The predicted gene structure including cleavage sites and an active C-terminal domain is present in humans. To date MSV mRNA has not been detected in

humans and the aim of this study was to determine whether MSV is expressed in humans.

Methods: qPCR was performed on a total RNA panel of pooled RNA (minimum 3 donors) from 20 different normal human tissues (Ambion) and specific primers designed for the predicted sequence of human MSV. All qPCR products were sequenced.

Results: No MSV mRNA was detected in any of the human tissues.

Conclusion: MSV mRNA was not detected in a selection of normal human tissues. Possible explanations include that MSV is not expressed in humans, that MSV is expressed but only in very low abundance or that MSV is only expressed at certain stages of development e.g. the linear growth phase at puberty, or during foetal development.

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