Projects beginning in 2002

2002/002

Genetic haemochromatosis and arthritis

Aims

We propose to analyse the relationship between genetic mutations in the HFE gene and the development of arthritis in the Busselton population using previously collected de-identified data. If this study confirms a role for iron in arthritis, given the high frequency of HFE mutations in the Australian population, this would potentially allow the rapid identification of individuals at risk of arthritis and may therefore have significant public health implications.

Investigators

- Prof John Olynyk, Dept of Medicine, UWA
- Dr Digby Cullen, Dept of Medicine, UWA
- Prof Matthew Knuiman, School of Population Health, UWA
- Dr Colin Sherrington, Dept of Gastroenterology, Fremantle Hospital

Project status

In progress

Publications


2002/003

An evaluation of the synergism between the Haemochromatosis gene mutations, iron and alcohol in alcohol-moderated liver injury in a prospectively studied Australian population.

Aims

a) To evaluate the synergism between the haemochromatosis gene, HFE mutations, iron and alcohol consumption in a well characterised cohort (3,011 individuals) of the Busselton population.
b) To assess the role of the haemochromatosis gene mutations in predisposing
to alcoholic liver disease.
c) To assess a possible role of the haemochromatosis gene in predisposing to heavy alcohol consumption.

Investigators

- Prof John Olynyk, Dept of Medicine, UWA
- Dr Digby Cullen, Dept of Medicine, UWA
- Prof Matthew Knuiman, School of Population Health, UWA
- Dr Colin Sherrington, Dept of Gastroenterology, Fremantle Hospital

Project status

In progress

Publications


2002/004

Characterising haemochromatosis gene mutations in the general population

Aims

The aim of the project is to determine the prevalence of novel genetic mutations in the Busselton Population in genes that control iron transport in humans. These genetic mutations include mutations in the iron transport genes termed ferroportin, transferrin receptor 1 and 2, and hepcidin. We have already completed analysis of the C282Y and H63D mutations in the HFE gene but wish to expand our analysis to include the other mutations as it has become apparent in the literature that there is a large range of phenotypic expressions of iron overload in hereditary haemochromatosis. In addition, a significant proportion of the general population who do not have haemochromatosis also have elevated serum iron studies. It is possible that these new genes may act as genetic modifiers of expression of haemochromatosis or may affect iron metabolism in individuals who do not possess mutations in the HFE gene.

Investigators

- Prof John Olynyk
- Dr Digby Cullen
2002/005

Thyroid dysfunction as a risk factor for fracture in the Busselton population

Aims

To determine whether hypothyroidism or hyperthyroidism as detected in sera from the 1981 survey are predictors of fracture, other falls-related injury, or mortality from fracture.

Investigators

- Assoc Prof Peter Leedman, Dept of Medicine, UWA
- Dr John Walsh, Dept of Endocrinology, SCGH
- Dr Peter O'Leary, Royal Perth Hospital
- Mr Satvinder Dhaliwal, Dept of Endocrinology, SCGH
- Dr Valdo Michelangeli, Bio-Mediq-DPC
- Peter Feddema, Bio-Mediq-DPC
- Gina Arena, School of Population Health, UWA
- Dr Laurie Lambert, School of Population Health, UWA

Publications

Walsh JP, Bremner AP, Bulsara MK, O'Leary P, Leedman P, Feddema PJ, Michelangeli V. 
**Subclinical Thyroid Dysfunction as a Risk Factor for Cardiovascular Disease.** Archives of Internal Medicine 2005; 165:2467-2472. [Abstract](#)

John P Walsh, Alexandra P Bremner, Max K Bulsara, Peter O'Leary, Peter L Leedman, Peter Feddema, Valdo Michelangeli. 
**Parity and the Risk of Autoimmune Thyroid Disease: A Community-Based Study.** J Clin Endocrinol Metab 2005; 90: 5309-5312. [Abstract](#)

Walsh JP, Bremner AP, Bulsara MK, O'Leary P, Leedman PL, Feddema P, Michelangeli V. 
**Thyroid dysfunction and serum lipids: a community-based study.** Clinical Endocrinology 2005; 63: 670-675. [Abstract](#)
2002/006

A longitudinal study of male androgen deficiency in the Busselton population

Aims

a) To determine the prevalence of male hypogonadism in aging men from the Busselton Population Survey.
b) Study the pattern of decline of testosterone levels with aging from subjects involved in both the 1981 and 1994/5 follow-up survey.
c) Evaluate the use of total testosterone compared with a calculated measure of non-SHBG bound testosterone (as a surrogate of bioavailable testosterone) in determining the prevalence of hypogonadism.
d) To study the relationship of testosterone levels and the rate of decline in testosterone levels to total and disease specific mortality in addition to morbidity associated with cardiovascular disease, hip fracture, prostate cancer and dementia utilising the linked mortality and WA Hospital Morbidity databases.

Investigators

- Dr Jonathan Beilin, Dept of Endocrinology and Diabetes, Royal Perth Hospital
- Assoc Prof Peter Leedman, Dept of Medicine, UWA
- Dr Peter O'Leary, Dept of Obstetrics and Gynaecology, KEMH
- Dr Valdo Michelangeli, Bio-Mediq-DPC

Project status

In progress

2002/007

Cancer mortality, folate and vitamin B12 status: the Busselton Health Study

Aims

To evaluate the association between serum folate, red cell folate and vitamin B12 levels in the 1969 Busselton survey cohort and the following:
1. subsequent death from any malignancy.
2. subsequent death from colorectal malignancy.
3. subsequent death from breast malignancy.
4. subsequent death from haematological malignancy.

Investigators
• **Dr John Beilby**, Dept of Clinical Biochemistry, PathCentre  
• **A/Prof Joe Hung**, Dept of Medicine, UWA  
• Dr Ric Rossi, Dept of Clinical Biochemistry, PathCentre  
• **Prof Matthew Knuiman**, School of Population Health, UWA

**Project status**

In progress

**Publications**

Rossi E, Hung J, Beilby JP, Knuiman MW, Divitini ML, Bartholomew HC. *Folate levels and cancer morbidity and mortality: Prospective cohort study from Busselton Western Australia.* *Ann Epidemiol* 2006; 16:206-212. [Abstract](#)

**2002/008**

**Iron and Cognition in Older Adults: A community population study**

**Aims**

The ongoing Busselton community study provides an unprecedented opportunity to investigate the effects of short-term and long-term iron deficiency or iron excess or haemochromatosis (HFE) gene mutations on cognitive impairment and dementia. We will survey participants from the 1994/5 survey of iron status and HFE genotype over 60 years of age in 2003/4 and living in Busselton or Perth. We will also follow up the survivors of the 1120 subjects who had memory testing in the 1987 survey of subjects over 65 years. In all we expect over 1000 participants. Iron studies and cognitive screening tests will be performed in all subjects, with clinical investigations for selected subjects. We will test for C282Y and H63D mutations in any subjects not already typed (notably those from the 1987 study) and will also determine APOE and transferrin genotypes for all subjects. Neuroimaging of selected subjects will identify brain lesions and quantify iron deposition. We will investigate the relationships of iron status and HFE mutations with mild cognitive impairment, demetia and brain abnormalities identified by neuroimaging. Clinical assessment will include full neurological examination, assessment of primitive reflexes, and measures of extrapyramidal function for any participants who fulfill any of the following criteria: dementia assessed by CAMDEX-R, dementia with Lewy bodies, frontoparietal dementia, stroke, minimal cognitive impairment and abnormal iron studies, homozygous for C282Y mutation.

**Investigators**

• **Prof John Olynyk**, Dept of Medicine, UWA
• Dr Liz Milward, School of Biomedical Sciences, University of Newcastle

Project status

In progress