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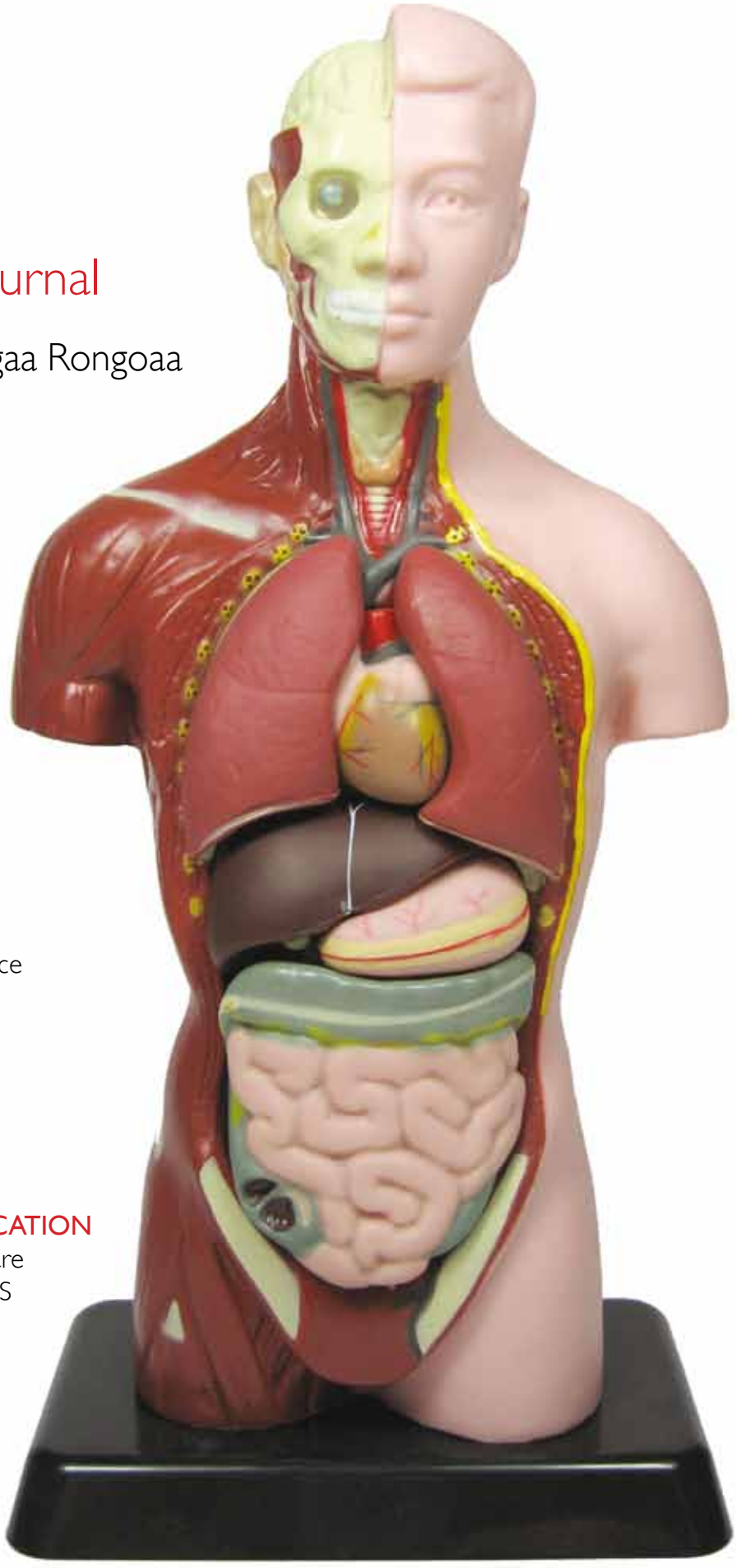

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EDITORIAL

Welcome to the tenth issue of the New Zealand Medical Student Journal (NZMSJ). The NZMSJ aims to support medical student professional development, to be a forum for opinions and discussion and to publish the educational writing of medical students. We feel that this issue achieves these aims, and in addition will make thought-provoking reading, due to the wide range of articles that reflect the diversity of New Zealand medical students.

This issue continues our tradition of showcasing the many examples of student involvement in global health and social issues. Congratulations must go to James Heaton, the winner of the Features Writing Prize, for his article, "Lessons in Humility on the Thai border". In this article, James describes the time he spent at the Shoklo Malaria Research Unit in Thailand. It is inspiring to read about the insight that was gained during this medical student's overseas experience in a situation that contrasts sharply with anything to be found in New Zealand.

As well as bringing you several articles on health provision in other countries, we also like to keep it close to home. In this issue you will find a comprehensive review of the rectal examination – "More than assessment of the prostate gland". The PR exam is one area of medicine that most medical students feel hesitant about, and it is therefore important to gain full understanding of its function and importance.

The NZMSJ executive would like to extend our sincere gratitude to Professor Peter Joyce, the Dean of the Christchurch School Medicine, for his generous sponsorship of this issue's Dean's Academic Writing Prize. The worthy recipient of this prize is Caroline Ulrich for her original research article entitled, "Risk stratification in patients presenting with chest pain who are not initially diagnosed with an Acute Coronary Syndrome". We also wish to thank Associate Professor David Perez for his continued invaluable contribution to our academic review process in his role as Academic Advisor.

Thanks must also go to the Faculty of Medicine, University of Otago and the New Zealand Medical Association for their support of the NZMSJ through their sponsorship of the launch function of the 10th issue of NZMSJ.

We would like to congratulate all of the authors published in this issue. Your initiative and efforts are admirable. We look forward to receiving such high quality submissions in the future.

The NZMSJ Executive

The NZMSJ editorial board maintains that the articles published under the heading "opinion" are the personal views of the author and the NZMSJ does not support or endorse these views in any way but respects the author's rights to voice his/her opinions.

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NZMSJ Academic Writing Prize
Issue 10
FIRST PLACE

Risk stratification in patients presenting with chest pain who are not initially diagnosed with an Acute Coronary Syndrome

Caroline Ulrich
Trainee Intern
Dunedin School of Medicine
University of Otago

Caroline is currently a trainee intern at the Dunedin School of Medicine. Having grown up in a rural community in South Canterbury, she has an interest in rural medicine and the limitations that smaller DHBs such as South Canterbury must cope with. She has now completed two summer research projects at Timaru hospital, both dealing with ways to best serve the predominantly rurally based population of South Canterbury and hopes to further her interest in rural medicine by working at a smaller hospital when she graduates this year.

ABSTRACT

Aims: Understanding outcomes for patients presenting with chest pain, determined not to be caused by an acute coronary syndrome (non-ACS), is important to aid triage and management. The primary intention of this study was to compare the clinical outcomes of non-ACS chest pain patients, divided into high-risk and low-risk non-ACS subgroups.

Methods: The hospital medical records of patients presenting to Timaru Public Hospital with non-ACS chest pain over a 4-month period (1/1/06 – 30/4/06) were reviewed. Eligible non-ACS patients were divided into high-risk and low-risk subgroups based on the presence or absence of a history of coronary artery disease (CAD), respectively.

Results: 128 patients with non-ACS chest pain were included in the final study group. Outcomes at a minimum of 18 months of follow-up differed significantly between the high-risk and low-risk non-ACS subgroups, especially the number of re-presentations (including acute coronary syndrome (ACS) and myocardial infarction (MI)). The high-risk non-ACS subgroup and patients with ACS chest pain were very similar with regard to outcomes such as re-presentations, ACS, MI and mortality.

Conclusion: This retrospective review provides evidence that outcomes for patients with non-ACS chest pain may be influenced significantly by a prior history of CAD. Furthermore, patients considered to be high risk, based on the presence of CAD, require more active investigation and invasive management followed by aggressive risk factor modification.

The presentation of chest pain to hospital is a common occurrence. While the management of acute coronary syndrome (ACS) -related chest pain is well defined, investigating and managing patients with chest pain initially thought to be of non-ACS origin, is less clear.

There is a wide variety of causes of non-ACS chest pain which include gastro-oesophageal disorders, pleuropericardial disease, pulmonary embolism, musculoskeletal pain as well as stress and anxiety-related disorders.[1-7] Several studies have recommended a range of investigations for these patients[1,3,7-10] which may be helpful in reaching a definitive diagnosis. However, such investigations are not always appropriate or available.

A recent retrospective cohort study published by Taylor et al[11] reported outcomes of patients who had attended a rapid assessment of chest pain clinic. This clinic was set up to reduce the number of hospital attendances and admissions by patients who did not have chest pain of coronary origin. In this study, patients were classified as "low risk chest pain" if they did not have ST-segment ECG change or symptoms suggestive of myocardial ischaemia on exercise[11] – similar to the protocol used to define "non-ACS chest pain" in this study. Results showed that only 3.6% of "low risk chest pain" patients suffered cardiovascular morbidity or mortality after six years of follow-up.[11]

Interestingly, a number of studies have previously concluded that a prior history of coronary artery disease (CAD) is important prognostically in patients with chest pain,[2,4,5] and is more important for long-term prognosis than discharge diagnosis[5]. Prina et al. (2004) found that patients presenting with chest pain and a history of CAD were more likely to have an adverse cardiac event within 12 months. They concluded that this should increase the clinician's level of suspicion that the pain could be coronary in origin, even with negative preliminary investigations.[2] Conversely, other studies have shown that patients with no prior history of CAD have better outcomes with respect to cardiac morbidity and mortality.[12,13]

The primary intention of this study was to look at clinical outcomes for patients presenting to hospital with chest pain of non-ACS origin (as defined over) divided into low-risk and high-risk non-ACS subgroups based on the presence or absence of a history of coronary artery disease.

METHODS

Study Design

Timaru Public Hospital (TPH) is a provincial hospital serving a population of 55000. All patients presenting to TPH with chest pain are triaged through the cardiac care unit (CCU). This study was a retrospective review of a consecutive sample of patients presenting with chest pain, determined to be of a non-ACS cause, between January 1 2006, and April 30 2006. Ethical approval was granted by the Regional Upper South A committee to conduct the study.

Study Population

The hospital medical records of all patients who presented to CCU with chest pain were reviewed to determine eligibility for the study. For the purpose of this study, ACS was defined as a presentation with chest pain associated with either:

1) ECG changes suggestive of ischaemia, (ST elevation or depression of >1mm in one or more leads or new T wave inversion)

or,

2) Positive cardiac enzyme Troponin T (TnT) of >0.03ng/ml during the

index admission.

All patients with a negative hospital evaluation for ACS, by the above criteria, were considered for this study. Exclusion criteria included:

1) An incomplete data set (less than two TnT results, no ECG or missing notes).

and

2) Residence outside the South Canterbury area.

The notes of patients presenting with chest pain due to ACS were reviewed to enable basic comparisons between the groups to be made. Patients admitted more than once during the four month study period with chest pain were included in this study at the first admission, and subsequent admissions were classified as re-presentations.

Study Protocol

To provide 18 months of follow-up, the review of patient notes began on November 9, 2007. The details of the index presentation including history, physical examination, demographic data, previously prescribed drugs and presence of cardiac risk factors were extracted from the hospital notes of each patient with non-ACS chest pain eligible for the study. Overall cardiovascular risk was determined by combining the total number of cardiac risk factors present in each patient with a maximum total of six. The risk factors used to determine this score were: proven history of CAD, family history of IHD/CAD, hypertension (>140/90mmHg; previously diagnosed +/- treatment), hypercholesterolaemia, diabetes (type I or II), smoker (past or present). Previous presentations and investigations for chest pain were also obtained from the notes. The final discharge diagnosis was taken from coding data. Patient notes were reviewed for any re-presentations to the CCU with chest pain, further investigations or treatment for chest pain, any new diagnoses that could account for the index presentation, and all-cause mortality.

Eligible patients with non-ACS chest pain were classified according to whether they had a definitive history of CAD or not. A history of CAD was defined as any previous: myocardial infarction (MI), percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass graft (CABG) or any combination of these. Two study subgroups were produced:

1) A low-risk subgroup of patients with no history of CAD.

2) A high-risk subgroup of patients with a history of proven CAD.

The notes of patients presenting with ACS chest pain were reviewed to extract basic demographic data (age, gender), details of any re-presentations and all-cause mortality.

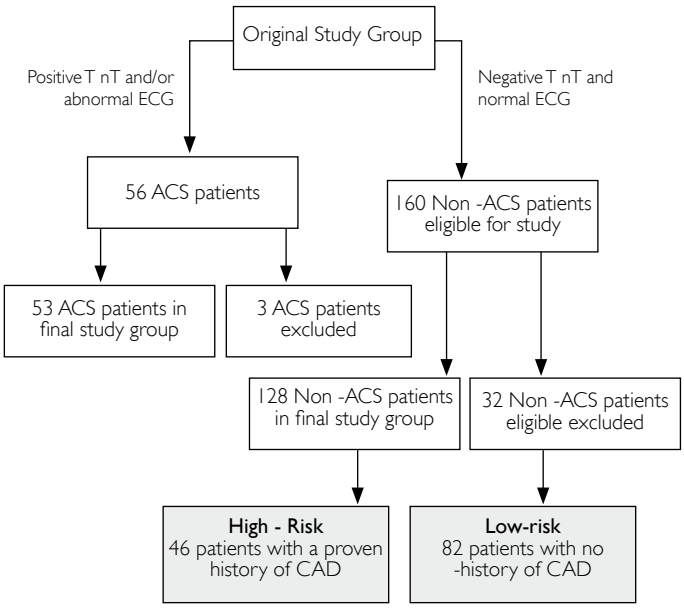
Data analysis

Nominal (categorical) data were summarised in percentages and independent-samples t-tests were used to identify statistically significant differences between the two study groups. Statistical analyses were performed using the SPSS software package (LEAD Technologies, Inc., 1989-2001).

RESULTS

During the study period, 216 patients presented to the CCU at TPH with chest pain. On review of all patient notes, a total of 160 (74%) patients were classed as having non-ACS chest pain. Of these, 26 (16%) patients were excluded due to incomplete data sets, and six (4%) were excluded due to their place of residence being outside the South Canterbury area. Of the remaining 128 patients, 46 had a proven history of CAD, 82 did not. Figure 1 shows the categorisation of the 216 patients presenting with chest pain.

Figure 1. Flow chart of 216 patients presenting to the CCU with chest pain



Baseline demographic characteristics of the two non-ACS groups and the ACS group are shown in Table 1. There was a statistically significant difference in mean age between the low-risk and high-risk non-ACS groups (95% CI of the difference = -16.5 to -5.9, p <0.0001). There was also a statistically significant difference between the low-risk non-ACS and ACS groups (95% CI of the difference = -16.2 to -5.7, p <0.0001). There was no difference in age between the ACS and high-risk non-ACS groups.

Table 1. Baseline demographic characteristics of all patients.

	Low-risk	High-risk	ACS
Number of patients	**82**	**46**	53
Mean age (range), yr	**60.2 (21-89)**	**71.4 (47-90)**	71.2 (38-93)
Female (%)	**45 (55%)**	**21 (46%)**	24 (45%)
Male (%)	**37 (45%)**	**25 (54%)**	29 (55%)

Cardiovascular risk factors present in both non-ACS chest pain patient groups are shown in Table 2. There was a statistically significant difference in mean cardiovascular risk between the low-risk and high-risk non-ACS subgroups (p<0.0001). Table 3 shows previously prescribed medications of all non-ACS chest pain patients.

Table 2. Cardiovascular risk factors of all non-ACS patients.

	Low-risk	High-risk
Positive family history IHD (%)	36 (**44%**)	25 (**54%**)
Preexisting hypertension (%)	38 (**46%**)	30 (**65%**)
Preexisting hypercholesterolaemia (%)	40 (**49%**)	25 (**54%**)
Preexisting Diabetes Mellitus (%)	12 (**15%**)	12 (**26%**)
Current Smoker (%)	11 (**13%**)	4 (**9%**)
Ex-smoker (%)	22 (**27%**)	29 (**63%**)
Mean cardiovascular risk *	1.95	3.73

IHD = Ischaemic Heart Disease

* Overall cardiovascular risk was determined by combining the total number of cardiac risk factors present in each patient, with a maximum total of six.

Table 3. Previously prescribed drugs of all non-ACS patients

Drug	Low-risk	High-risk
Nitrate	5%	37%
Beta-blocker	21%	59%
Calcium channel blocker	11%	17%
Diuretic	5%	37%
Aspirin	22%	78%
ACE inhibitor	7%	30%
AT II receptor blocker	0	13%
Antacid	4%	4%
H2-antagonist	1%	2%
Proton Pump Inhibitor	18%	43%
Statin	16%	72%
Fibrate	1%	0

ACE = Angiotensin Converting Enzyme; AT = Angiotensin

Mean length of stay for evaluation was 1.31 days (SD 1.71, range 0 to 8) in the low-risk non-ACS subgroup, and 1.37 days (SD 1.25, range 0 to 5) in the high-risk non-ACS subgroup. Discharge diagnoses for both groups are shown in Table 4.

All patients were followed for at least 18 months. The average duration of follow-up was 623 days (SD 30.8, range 561 to 670) in the low-risk subgroup, and 622 days (SD 29.3, range 560 to 692) in the high-risk subgroup. The difference in the mean number of re-presentations (Table 5) was significant between the low-risk and high-risk non-ACS subgroups (95% CI of the difference -1.928 to -0.759, p<0.0001). Similarly, between the low-risk non-ACS subgroup and ACS group (95% CI of the difference -1.067 to -0.278, p=0.001). There was no significant difference between the high-risk non-ACS subgroup and the ACS group (95% CI of the difference -0.120 to 1.536, p=0.093). Table 5 shows the outcomes of patients at a minimum of 18 months follow-up. Causes of mortality in the low-risk non-ACS subgroup included: two of unknown cause, and one small cell carcinoma of lung. In the high-risk non-ACS subgroup, causes of mortality included: three of unknown cause, one electromechanical dissociation, and one bronchopneumonia secondary to myelodysplasia.

Table 5. Outcomes during minimum 18-month follow-up.

Outcome	Low-risk	High-risk	ACS
No. representing to CCU (%)	17 (21%)	22 (48%)	23 (43%)
Mean no. representations	0.31	1.7	0.98
No. representing with ACS (%)	1 (1%)	8 (17%)	12 (23%)
All-cause Mortality (%)	3 (4%)	5 (11%)	9 (17%)

DISCUSSION

Approximately 800 patients present annually with chest pain to CCU at Timaru Public Hospital. Based on this study, 74% of these patients will have non-ACS chest pain. While the percentage of patients determined to have non-ACS chest pain is larger than that found in other studies,[1-3] this reflects the criteria used to determine patients eligible for the study. A number of patients who may have had unstable angina, despite normal ECG and serial cardiac enzymes, were included in the non-ACS chest pain group.

Our study had some limitations:

1) Being a retrospective study we relied on the completeness of hospital notes for historical data.
2) The study population was predominantly European, therefore our findings may not be generalisable in locations where there is greater

Table 4. Discharge diagnoses of all non-ACS patients.

	Low-risk	High-risk
Chest Pain of undetermined cause	30 chest pain NOS 9 non-cardiac chest pain 2 musculoskeletal chest pain 2 atypical chest pain 1 sinus tachycardia **= 44 (54%)**	9 chest pain NOS 3 non-cardiac chest pain 1 musculoskeletal chest pain **= 13 (28%)**
Gastrointestinal-biliary cause	4 GORD 3 gastritis 2 oesophagitis **= 9 (11%)**	1 GORD 1 gastritis 1 epigastric pain NOS **= 3 (7%)**
Respiratory cause	1 LRTI 3 pleuritic chest pain 1 infective exacerbation asthma **=5 (6%)**	2 LRTI **= 2 (4%)**
Coronary artery disease	4 angina 8 unstable angina **= 12 (15%)**	17 angina 6 unstable angina **= 23 (50%)**
Other	3 LVF/CHF/RVF 2 PAF 2 recurrent SVT/WPW 2 pericarditis 1 PE 1 angina 2° anaemia 1 mechanical pain (due to displaced spinal screws) **= 12 (15%)**	1 LVF 1 PAF 1 VT 1 angina 2° anaemia 1 aortic stenosis **= 5 (11%)**

NOS = Not Otherwise Specified; GORD = Gastro-oesophageal Reflux Disease; LRTI = Lower Respiratory Tract Infection; LVF = Left Ventricular Failure; CHF = Congestive Heart Failure; RVF = Right Ventricular Failure; PAF = Paroxysmal Atrial Fibrillation; VT = Ventricular Tachycardia; PE = Pulmonary Embolism; SVT = Supraventricular Tachycardia; WPW = Wolff-Parkinson-White.

ethnic diversity.

3) An inability to extend follow-up to the community meant that a complete picture of healthcare resource utilisation by these patients was not able to be achieved.

This study shows that patients presenting with chest pain initially diagnosed as non-ACS can be divided into low-risk and high-risk subgroups based on the presence or absence of a prior proven history of CAD. This supports the conclusion, of Launbjerg et al. (1994), that patients of higher risk can be more readily identified from the medical history than discharge diagnosis.[5]

Patients in the high-risk non-ACS subgroup were very similar in terms of age and gender balance to those patients who were initially found to have ACS chest pain. Patients in the low-risk non-ACS subgroup were significantly younger than both the high-risk non-ACS subgroup and the ACS group. The proportion of females was higher in the ACS group, which is consistent with other studies of patients with chest pain of non-coronary origin.[1,2,6]

Greater than half of the low-risk non-ACS subgroup had a discharge diagnosis of chest pain of undetermined origin, whereas 50% of the high-risk non-ACS subgroup had a diagnosis of either angina or unstable angina. The low-risk non-ACS subgroup did, however, have a high percentage (15%) of other diagnoses (Table 4.) that have previously been shown to carry significant morbidity and mortality.[4]

At a minimum of 18-months follow-up, outcomes were significantly different between the low-risk subgroup and the high-risk non-ACS subgroups (Table 5). The high-risk non-ACS subgroup had a greater number of patients re-presenting with chest pain, a higher mean number of re-presentations, and a greater number of patients presenting with ACS and MI, all of which are comparable to the ACS group. These findings are consistent with the conclusion made by Prina et al that in any patient who has a past medical history of cardiac disease, clinical suspicion of an ACS must remain high even in the absence of ischaemic ECG changes or raised cardiac enzymes.[2] This concept is further supported by the 2007 ACC/AHA Guidelines for the Management of Unstable Angina/Non-ST Elevation Myocardial Infarction. Here a history of CAD, including MI, is listed as a feature indicative of a high likelihood that the signs and symptoms the patient presents with are due to ACS secondary to CAD.[14]

Structured scoring systems to determine the subsequent risk of cardiac events, such as the Thrombolysis in Myocardial Infarction (TIMI) risk score, would be a useful way of objectively determining risk in patients presenting with chest pain, even in those who are thought to not have ACS. Both an objective history of CAD and cardiovascular risk factors (>3) are included in this risk score, and it is therefore likely to help identify patients with high-risk non-ACS chest pain (as defined in this study) and improve outcomes for these patients. Furthermore, the implementation of an algorithm for patients suspected of having ACS, such as that published in the 2007 ACC/AHA Guidelines[14], could be a useful addition to the use of a structured risk scoring system. Both of these tools would provide a structured protocol for the identification and management of patients with chest pain and most likely lead to improved outcomes for all patients.

CONCLUSION

For patients presenting to hospital with chest pain of non-ACS origin, this study suggests that stratification into high-risk and low-risk subgroups is useful. The presence or absence of a prior history of CAD is a simple method of making these respective classifications and could be achieved using a structured risk scoring system such as TIMI. Low-risk non-ACS patients were unlikely to represent with an adverse cardiac event, but high-risk non-ACS patients had outcomes comparable to patients with ACS chest pain. In particular, the high rate of representations is indicative of the need to carefully investigate and follow patients considered to be at high risk.

ACKNOWLEDGEMENTS

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The role of mitochondrial dysfunction in Parkinson's disease

Dasha E. Nelidova
4th year Medical Student
School of Medicine
University of Auckland

Dasha is a 4th year medical student at the University of Auckland. Her research interests are in the area of cell regeneration.

INTRODUCTION

Parkinson's disease (PD) is a prevalent neurodegenerative movement disorder, affecting 1% of those aged over 60 [reviewed in Abou-Sleiman et al., (1)]. As substantia niagra (SN) dopamine neurons degenerate, patients begin to struggle with initiation and maintenance of movement. Rigidity, postural instability and a characteristic resting tremor ensue. Associated with areas of neuronal degeneration are intra-cytoplasmic inclusions containing alpha-synuclein protein (Lewy bodies) (2). Degeneration of nigral projections to the striatum is gradual and patients become symptomatic when striatal dopamine (DA) levels get down to about 30% of normal (3). Sporadic idiopathic disease accounts for 95% of cases and tends to be of late-onset , while familial cases have been linked to mutations in the genes for alpha-synuclein, parkin, PINK1, DJ1 and others (1).

The pathogenesis of idiopathic PD appears to involve multiple processes. Neuroinflammation, excitotoxicity, oxidative stress, environmental toxins and accumulation of misfolded proteins from proteasomal impairment are likely responsible (4,5).This review will present evidence for the involvement of mitochondria in PD and discuss how mitochondrial dysfunction leads to neuronal dysfunction and death.

Mitochondria modulate many cellular processes. Adenosine triphosphate (ATP) is generated as electrons are passed along the protein complexes of the mitochondrial electron transport chain. Mitochondria sequester surplus cytoplasmic Ca^{2+} and play a role in neutralisation of free radicals. However, mitochondrial processes themselves produce much of the cell's free radical load, while release of certain mitochondrial factors into the cytoplasm is enough to trigger apoptosis.

EVIDENCE FOR THE ROLE OF MITOCHONDRIA IN PARKINSON'S DISEASE

Dysfunction of Complex I of the mitochondrial electron transport chain leads to a Parkinsonian phenotype

Mitochondrial dysfunction became a suspect in Parkinson's aetiology after a case of illicit drug use. A dose of 1-methyl-4-phenyl-1,2,3,4-tetrahydropyridine (MPTP) injected intravenously created parkinsonism in humans (6). It was later discovered that MPTP's active metabolite, 1-methyl-4-phenylpyridinium ion (MPP+), was able to selectively accumulate in dopamine neurons after uptake by the dopamine transporter. In the neuron MPP+ inhibited complex I of the mitochondrial electron transport chain (1). In fact, MPTP complex I inhibition is now used to induce PD in animal models.

Indeed, further investigation demonstrated a significant decrease in complex I activity in post-mortem human PD brains (7), as well in skeletal muscle and platelets of the patients (8, 9). This systemic defect in complex I is perhaps a result of a genetic flaw or exposure to a mitochondrial toxin during life.

Mitochondrial DNA deletions and particular polymorphisms accompany Parkinson's disease

Mitochondrial DNA codes for many proteins of the electron transport chain. Acquired mitochondrial DNA (mtDNA) deletions that can expand clonally are observed in individual PD involved neurons, although they are also found at high levels in normal aged neurons (10). There does not seem to be a difference in the number of acquired point mutations in mtDNA between PD and controls (11, 12). Instead, mitochondrial polymorphisms that increase relative uncoupling of mitochondria have been found to decrease the risk of developing PD (13). Uncoupling refers to the dissipation of the proton gradient across the inner mitochondrial membrane, which keeps oxidative phosphorylation induced free radical production in check. Uncoupling protein- 2 (UCP-2) knock-out mice are predisposed to niagral neurodegeneration, probably from changes in reactive oxygen species buffering ability, while UCP-2 overexpressing animals are resistant (14). Polymorphisms in mtDNA can explain why PD is so strongly associated with ageing (15), as they lead to small changes in the efficiency of mitochondrial oxidative phosphorylation and free radical generation, which accumulate over the lifetime of the person and account for the degree of neuronal cellular ageing and therefore the risk of developing PD.

Mutations in nuclear DNA affect mitochondrial function and account for familial Parkinson's disease

Nuclear DNA codes for most mitochondrial proteins. PTEN induced putative kinase-1 (PINK1) is a mitochondrial kinase that normally protects against cell death by controlling cytochrome c release from mitochondria (16). Loss of function mutations in the PINK1 gene can be rescued by wild type parkin (ubiquitin E3 ligase and component of the ubiquitin-proteasome system that performs ATP-dependent protein degradation) acting downstream of PINK1 to prevent mitochondrial swelling and cytochrome c release (13). PINK1 or parkin loss of function mutations can lead to autosomal recessive juvenile PD (17, 18).

Mutations in the alpha-synuclein gene lead to aggregation of the protein and autosomal dominant PD (19). Alpha-synuclein knock-out mice are resistant to MPTP induced neurotoxicity, suggesting that the sequelae of complex I inhibition may include derangements in protein handling. The development of mitochondrial pathology with overexpression of mutant alpha-synuclein (20) demonstrates the connection between abnormal nuclear DNA derived mitochondrial proteins and mitochondrial dysfunction.

DJ-1 is a peroxiredoxin-like peroxidase that scavenges excess H_20_2 (21), therefore DJ-1 loss of function mutations lead to decreased protection against apoptosis. Leucine-rich repeat kinase-2 (LRRK2) mutations account for 1-2% of late-onset sporadic PD cases (13). Protein phosphorylation of mutated LRRK2 and PINK1 contributes to protein mishandling that is a key part of PD pathogenesis (22). Proteolytic stress and abnormal phosphorylation of mitochondrial proteins likely affect the function of mitochondria themselves (23).

DOWNSTREAM CONSEQUENCES OF MITOCHONDRIAL DYSFUNCTION

Mitochondrial reactive oxygen species lead to oxidative stress and altered cell signalling

Mitochondria are central to the generation of reactive oxygen and nitrogen species and integration of pro- and anti-apoptotic signals in the cell (24). Mitochondrial ROS generation and maintenance of antioxidant defences are dependent upon the redox and energetic state of the cell (13). Complex I dysfunction increases ROS production by interrupting the flow of electrons along the electron transport chain. Complex I dysfunction likely also lowers the threshold for apoptosis in PD (23, 25).

Indeed, post-mortem analysis of PD affected brains showcases oxidative damage to lipids, proteins and DNA (26). Mitochondria themselves can become susceptible to the ROS they generate if their pool of reduced glutathione becomes depleted (27). Glutathione normally donates electrons to ROS in order to achieve neutralisation; however one of the earliest changes in PD is a marked decrease in niagral glutatione (28).

Production of ROS by mitochondria can also have an effect on signal transduction in the cell (24). Mitochondria generate most of the cell's superoxide radicals as electrons escape to join molecular oxygen prematurely (28). Because of the high activity of Manganese-superoxide dismutase within mitochondria, much of the superoxide is converted to H_20_2, however H_2O_2 can permeate through the mitochondrial membrane into the cytoplasm (25). There it can regulate dopamine transmission of the niagro-striatal pathway via the activation of ATP-sensitive K^+ channels (29).

Dopamine release, neuronal death and K_{ATP} channels

K_{ATP} channels are downstream of complex I, and are controlled by mitochondrial metabolism. Activation depends on the degree of mitochondrial uncoupling and ROS generation (30) and is mediated by H_2O_2. Activation of glutamatergic AMPA receptors on medium spiny neurons of the dorsal striatum enhances mitochondrial generation of H_2O_2, which then diffuses to DA terminals to open K_{ATP} dependent channels and inhibit DA release (29). K_{ATP} channels are selectively activated in response to complex I inhibition in the SN but not in ventral tegmental area (VTA) dopamine neurons, likely accounting for the preferential degeneration of SN neurons in PD (30). K_{ATP} channel subunit $Kir_{6.2}$ knockout mice were protected against MPTP induced neurodegeneration in the SN (30), showing that the activation of this channel perhaps mediates cell death of DA neurones in PD.

Therefore, overproduction of H_2O_2 by mitochondria can lead not only to oxidative damage but also to decreased release of DA in the striatum. Depleting levels of DA will result in an increased suppression of the ventral lateral nucleus of the thalamus and subsequent decrease in the excitatory input to the motor cortex, leading to the physical symptoms of PD. Differential degeneration of SN and not VTA dopamine neurons in PD, can be explained by activation of K_{ATP} channels.

Mitochondrial K_{ATP} channels and mitochondrial Ca^{2+} regulation

Mitochondrial are important in Ca^{2+} homeostasis as they sequester excess cytoplasmic Ca^{2+} (27). Cytoplasmic Ca^{2+} is implicated in activation of Ca^{2+} dependent enzymes and apoptosis. Ca^{2+} accumulation in mitochondria can affect ATP synthesis and decreased ATP synthesis will in turn decrease the removal of Ca^{2+} from the cytoplasm by ATP requiring ion pumps (27). Oxidative stress together with Ca^{2+} and phosphate is thought to open the mitochondrial transition pore, leading to the release of cytochrome c into the cytoplasm and also to mitochondrial swelling (31).

Mitochondrial K_{ATP} channels sit in the inner mitochondrial membrane and lead to the depolarisation of the mitochondria, unlike plasma membrane K_{ATP} channels that hyperpolarise the cell (31). Depolarisation leads to protein kinase C activation, which activates ROS scavengers and promotes the synthesis of other anti-ROS proteins (31). Preventing swelling of the mitochondria limits Ca^{2+} influx and thus preserves efficiency of respiration (31). ROS can activate mitochondrial K_{ATP} channels (31); however uncontrolled ROS production may modify the channel so that its function is compromised. Agents that control Ca^{2+} entry into the cytosol (dihydropyridines), as well as agents that activate mitochondrial K_{ATP} channels to limit Ca^{2+} accumulation in mitochondria, are neuroprotective (15, 31).

Mitochondria-dependent apoptosis in PD

Cytochrome c and apoptosis-inducing factor (AIF) can be released from mitochondria into the cytoplasm to trigger cell death (27). Translocation of AIF to the nucleus leads to nuclear alterations such as chromatin condensation and large scale DNA fragmentation (27). Cytochrome c interacts with apoptotic protease activating factor (Apaf-1), encouraging Apaf-1 to bind procaspase-9, which initiates procaspase-9 cleavage to its active protease form. Caspase-9 goes on to cleave and activate caspase-3 (27).

It is believed that the death of dopamine neurons in PD is mediated via the cytoplasmic actions of mitochondrial cytochrome c. Cytochrome c is normally bound by anionic phospholipids, primarily cardiolipin, to the inner mitochondrial membrane (32). Complex I induced disruption of mitochondrial respiration blocks electron flow along the mitochondrial transport chain and produces ROS. These oxidatively modify cardiolipin and increase the soluble pool of cytochrome c in the mitochondrial intermembrane space (32). Discharge of accumulated cytochrome c into the cytoplasm is dependent upon proapoptotic Bcl-2 family member Bax (32). Bax permeablises the outer mitochondrial membrane allowing cytochrome c to leak into the cytosol. DNA damage from ROS activates transcription factor p53 and c-Jun N-terminal kinase (JNK) pathways, acting through BH3-only protein Bim (26). P53 is responsible for inducing transcription of Bax, while Bim mediates translocation of Bax from the cytosol to the mitochondrion.

Therefore a self-amplifying cascade is set up, starting with mitochondrial dysfunction and increased ROS production and ending at mitochondrial liberation of cytochrome c and activation of apoptotic mediators such as caspases. Attenuation of mitochondrial-dependent apoptosis can be achieved by targeting cytochrome c or Bax, however it is important to note that neurons have separate self-destruct programmes for cell bodies and axons (33). Axonal degeneration is caspase independent and likely begins before soma degeneration (33). The contribution of axonal degeneration to PD symptom development needs elucidating.

CONCLUSION AND THERAPEUTIC IMPLICATIONS

Dopamine neurons are under significantly more stress than other neurons because the metabolism of dopamine is in itself associated with reactive oxygen species generation (4). Reliance on L-type Ca^{2+} channels for pacemaker activity leads to Ca^{2+} accumulation in mitochondria which comes at an energetic cost (15). It is not surprising that SN neurons are lost at a much higher rate even with normal aging (15). PD may represent an acceleration of the normal aging process due to complex I dysfunction and resultant increase in ROS production that ultimately leads to mitochondrial DNA and protein damage, and later, to cell injury and death. Most toxins used to model PD such as MPTP, 6-hydroxydopamine (6-OHDA), paraquat and rotenone achieve niagro-striatal degeneration by means of overproducing ROS and increasing oxidative stress (25).

Genetic causes of PD supports the notion that mitochondrial dysfunction, oxidative stress and proteasomal system dysfunction are interdependent and interact to influence each other and to contribute to the parkinsonian phenotype. Genetic mutations, polymorphisms and environmental toxins likely contribute to oxidative stress and mitochondrial dysfunction. Mitochondrial-dependent apoptosis seems to be the end point of all insults. Targeting mitochondria to modify the course of PD is currently being explored.

MitoQ aims to mimic endogenous mitochondrial co-enzyme Q10 to achieve an anti-apoptosis and anti-oxidative stress effect (34). The efficacy of this orally active antioxidant in slowing the progression of Parkinson's is being tested in Phase III clinical trials. Creatine for enhancement of mitochondrial energy production is also in trials. Although some investigators

document no improvement of the Unified Parkinson's Disease Rating Scale score (35, 36), Neuroprotection Exploratory Trials in Parkinson Disease (NET-PD) have deemed both compounds worthy of further study (37, 38). This lack of clear success, however, has led to some questioning the primary importance of mitochondrial impairment, particularly oxidative stress, in the pathogenesis of Parkinson's disease (39). It is likely that individuals do vary in the relative contribution of mitochondrial dysfunction to their disease onset and progression. Identification of those in whom mitochondrial derangement plays the greatest role may represent the next stage of Parkinson's treatment, as these are the people who may benefit most from pharmacological mitochondrial agents.

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Primary characterization of a prolactin receptor dominant negative mutant using PC12 cell line

Sultan Al-Shaqsi
Bachelor of Medical Science Student
Centre for Neuro-Endocrinology
University of Otago

Sultan Al-Shaqsi is a medical student doing a BMedSci (Hon) in Emergency Medicine. He believes Emergency Medicine is all about "you know what to do when you don't know what to do". This article is a result of a summer studentship in 2007/2008.

ABSTRACT

Prolactin is a multi-functional peptide hormone produced and secreted by the anterior pituitary gland. In addition to its traditional role, the action of prolaction has been implicated in many other physiological and pathological processes. The aim of this project was to investigate the effectiveness of a newly developed dominant negative prolactin receptor using phaeochromocytoma (PC12) cell line. The response of PC12 cells to prolactin stimulation was tested using immuno-staining for STAT1 and p-STAT3 which are proteins in the activation pathway of prolactin. Preliminary results indicate there was a difference between the prolactin stimulated PC12 cells and the control, thereby providing information for future investigations.

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INTRODUCTION

Prolactin (PRL) is a peptide hormone primarily associated with lactation and, is synthesised and secreted mainly by lactotrope cells in the adenohypophysis[1]. PRL has a range of physiological actions including the stimulation and maintenance of mammary tissue during lactation[1]. Furthermore, it is appreciated that PRL has diverse roles in many other physiological processes such as osmoregulation, behaviour, immunity and growth[2]. In addition, PRL has been shown to be involved in pathological conditions associated with cancer and sexual dysfunction[3]. A recent study demonstrated that the appearance of genetically-induced mammary tumours is delayed in mice with PRL deficiency; whereas PRL transgenic mice spontaneously develop mammary neoplasia indicating that inhibition of PRL may have a role in anti-tumour therapy.

Prolactin receptors (PRLr) are widely expressed on a range of tissues and cells including breast epithelia, prostate cells and lymphocytes[4]. The PRLr belongs to the class I cytokine receptor family and contains an extracellular binding domain, a single transmembrane domain, and an intracellular domain required for signal transduction, mainly via Janus Kinase2 / signal transducer and transcription activator 5 (JAK-2/STAT5). In addition, other pathways that includes STAT1/STAT3 pathway also play a role in prolactin mechanism cascade as illustrated in the diagram below (Figure 1). The PRLr in humans has been shown to have three isoforms (long, intermediate and short) . Prolactin exerts its effect through binding to the extracellular domain of the receptor which induces dimerisation[5], leading to the activation of a protein tyrosine kinase (Jak2), which is non-covalently associated with the cytoplasmic domain of the prolactin receptor. Jak2 phosphorylates Stat5 which dimerises and translocates to the nucleus where it specifically binds to sequence elements in the promoter regions of genes and initiate cellular responses accordingly.

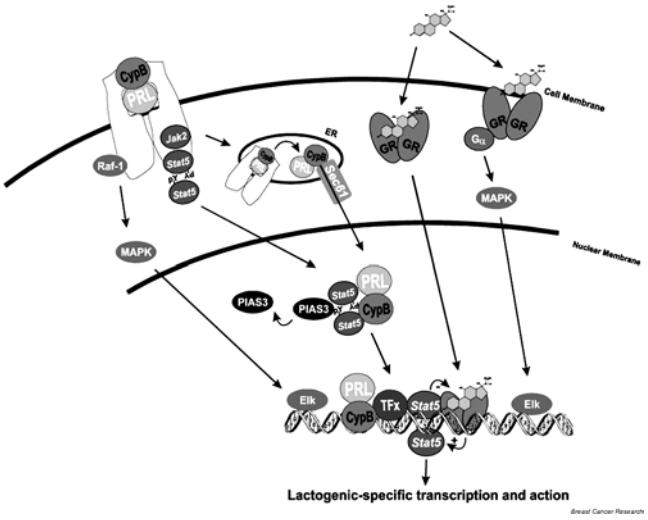


Figure 1: PRL hormone action and its transcription cascade (adopted from Breast Cancer Research Journal).

Understanding PRL's diverse actions has been limited by the lack of effective receptor antagonists and a model with a mutant PRLr (dominant-negative) which would be an ideal control model for future research of prolactin. This research investigates the use of cell cultures to test the effectiveness of this recently developed dominant-negative prolactin receptor. A dominant negative PRLr has been designed and inserted into a pEGFP-N2 vector. When transfected, this vector will express green fluorescent protein (GFP) and the mutant receptor. Phaeochromocytoma (PC12) cells are known to endogenously express PRLr[3]. In response to PRL stimulation these cells have been reported to exhibit an activation of Jak2/STAT3 pathway and undergo a proliferative response[3] which can be quantified. In the current project, PC12 cells were transiently transfected with dominant-negative PRLr and stimulated with PRL. The response to PRL stimulation was monitored by staining for STAT1 and phosphoraylated-STAT3 proteins. This study was the first attempt to characterize dominant negative PRLr in a cell culture.

METHODS

Bacterial transformation.

The vector was generously donated by Dr Paul Le Tissier (National Institute for Medical Research, UK). DNA was eluted from filter paper in 50 µl Milli-Q water. This was left for five minutes then centrifuged for four minutes at 14,000g. From the extracted DNA, 2µl was used to transform cells while the rest was frozen at -80 °C. Ultra-competent E.Coli cells (One Shot® TOP10 from Invitrogen) were thawed on ice, then, 2µl of DNA added and mixed gently. The cells were left on ice for 30 minutes and heat shocked at 42°C for 30 seconds. Next, 250µl of pre-warmed Super Optimal Broth (SOB) was added and incubated for one hour at 37°C in a shaking water bath. Aliquots of 20µl, 50µl and 100µl of cells were plated onto three Luria-Bertani (LB) neomycin-containing agar plates. The plates, and an empty plate (control), were incubated for 72 h at 37°C. After that, a single isolated bacterial colony was collected using a pipette tip, and transferred to LB broth containing neomycin and grown for 48h in 37°C incubator. The resultant bacterial culture was centrifuged for 10 minutes at 4,000g and DNA isolated using MAXI prep (PureLink™HiPure) according to the manufacture's protocol.

Restriction enzymes analysis

1.2% agarose gel was used in this analysis and formulated using a standard agarose preparation. Purified DNA samples were incubated with different restriction enzymes (EcoRI, BamHI, NcoI and HindIII). With a final volume of 10µl each combination consisted of 8µl DNA sample and 2µl of restriction enzyme. The 50bp and 1kbp DNA ladders were from Invitrogen and the Bench Top 1kbp DNA was from Promega. DNA ladders consisted of 2µl dilution buffer, 1µl DNA ladder and 9µl Tris-Borate-EDTA (TBE) buffer. 10µl of sample and DNA ladders were run on the agarose gel at 130 V and 60 mA for two hours. Bands then located under UV transilluminator and a Polaroid photograph taken.

PC12 cell culture

Plate collagen coating: plates were coated with 6-10 µg/cm of 0.01% collagen solution (Sigma C 8919) and then rinsed with Milli-Q water prior to cells plating. A frozen PC12 cell stock was quickly thawed in 37°C water bath. Pre-warmed complete RPMI medium was added and the cells centrifuged at 220g at room temperature for five minutes. Next, 5ml of RPMI was added and cell were re-suspended and plated at about 1×10^7cells per well. Cells were maintained at a 37°C and 5% CO2 environment. In this project PC12 cells were fixed using -20 °C methanol by removing the RPMI medium and gently adding -20 °C methanol for five minutes at room temperature. Methanol was then aspirated and the cells left to dry for one hour.

PC12 cell transfection.

Before the day of transfection, cells were deprived of complete medium and grown in serum-free medium. The density of cells was calculated to be around 8×10^3 cell per well in 96-well plates. DNA (40ng, 200ng and 500ng) was diluted in 20µl of serum-free (SF) medium. Lipofectamine ™LTX Reagent from Invitrogen (0.35µl) was added to the 20µl DNA-containing medium and left for 25 min at room temperature to form DNA-lipofectamine complexes. To each well, a 100µl of fresh SF medium was added and 20µl of DNA-Lipofectamine complex added and the cells incubated at 37°C, 5% CO2 for 48h. Transfection was observed under fluorescent microscope using appropriate optics for GFP.

PC12 cell stimulation with prolactin

Cells were plated at density of about 100,000 per well on collagen-coated cover slips contained in 24-well plates two days prior to stimulation. Cells were rinsed twice with HEPES buffer at 37°C. Some cells were treated with 10nM of ovine PRL (Sigma L6520) for 15 minutes whereas other cells were incubated with HEPES buffer only. Cells were fixed using -20°C methanol as described above. After fixation, cells were blocked with 4% goat serum/phosphate buffer saline (GS/PBS) for one hour and then incubated with primary antibody against STAT1 (Biosource™) or p-STAT3 (Biosource™) at a dilution of 1:200 and 1:100 in GS/PBS, respectively, at 4°C for 48h. Goat anti-mouse secondary antibody (Alexa Fluor 488) was used to label the primary antibodies. The secondary antibody was incubated for 90 minutes at room temperature under reduced light exposure. The cover-slips then rinsed with Milli-Q water, mounted with Vectashield and viewed under fluorescence microscopy.

Fixation of PC12 cells for immuno-localization was with -20°C methanol or 8% para-formaldehyde (used in preliminary experiments) which preserved more cells and reduced the washing effect on cells compared with room-temperature 70% ethanol(data not shown in this article). However, in this research -20°C methanol was superior to 8% para-formaldehyde because rapid fixation was required to rapidly preserve immunocytochemical events occurring as a result of PRLr activation.

RESULTS

Cell transformation and vector amplification

Ultra-competent cells transformed successfully following the protocol described in the Methods. On the third day of incubation with DNA, colonies of cells were growing in a volume-dependent fashion. The 100µl agar plates had 8 distinct colonies compared to 5 in 50µl and 2 in 20µl plate. The control plate grew no observable colonies. The average absorbance ratio at 260/280nm wavelengths was 1.82 which is consistent with reference range for pure DNA (1.8-2.0). The quantity of DNA extracts was 147ng/µl and 145ng/µl for the separate preparations.

Restriction enzymes analysis of purified DNA

Samples of DNA were tested to verify the presence of the construct of interest using restriction enzymes (EcoRI, BamHI, NcoI and HindIII). The uncut sample gave a fragment of 5.7kbp (Lane A, Figure 2) which was as expected from uncut vector containing the construct (Figure 3). The use of EcoRI and BamHI, which demarcated the insert region (Figure 3), gave two fragments of about 1kbp and 4.6kbp (Lane B, Figure 2). Similarly, the use of HindIII and BamHI enzymes, which also enclosed the insert region (Figure 3), gave two bands with 1kbp and 4.6kbp (Lane E, Figure 2). The two fragments from both combinations of restriction enzymes matched the expected values for the vector and the construct. Furthermore, using NcoI restriction enzyme which has three recognition sites in this vector, gave three bands of the expected size about 2kbp, 1kbp and 700bp (Lane C, Figure 2). In addition, XbaI restriction enzyme which has one recognition site in this vector was tried and gave one fragment which looks similar to the uncut DNA (Lane D, Figure 2).

Figure 2: Restriction enzymes analysis Polaroid photograph.

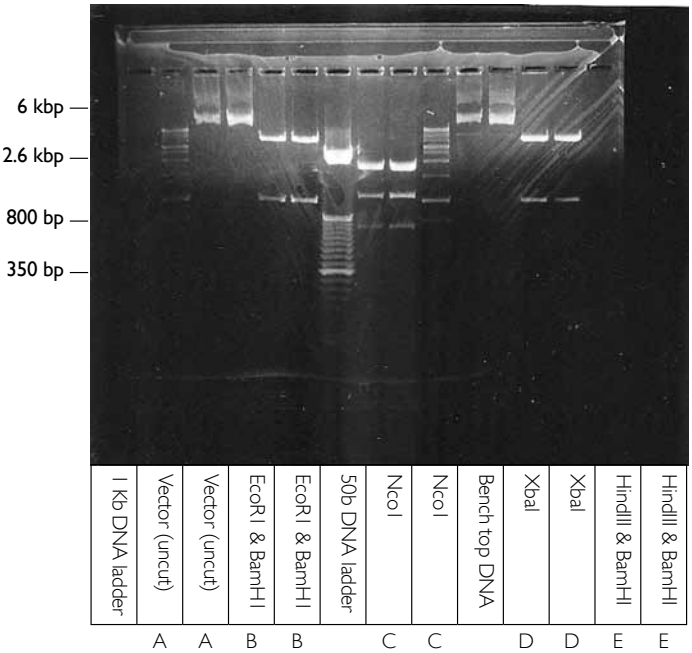


Figure 3: p EGFP-N2 vector.

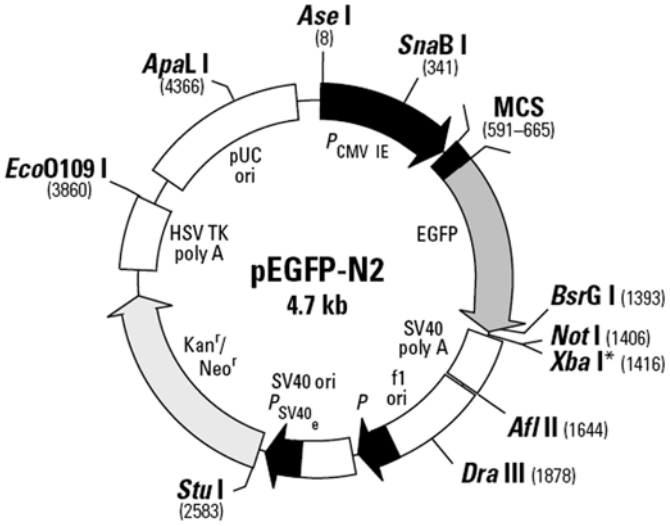


Figure 4: Two transfected PC12 cells showing green fluorescent due to p-EGFP-N2 after 48 hours.

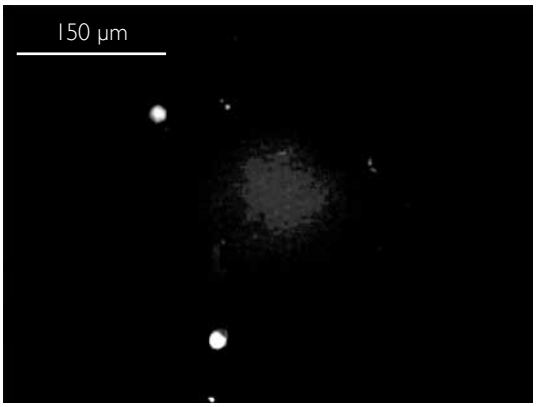


Figure 5: Basal cells stained for STAT1.
Uniformly cytoplasmic staining with difference in intensity between cells.

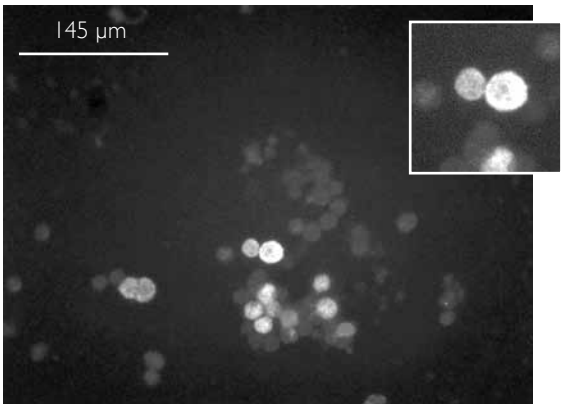


Figure 6: Prolactin-stimulated cells stained for STAT1.
The arrow indicate two cells with finely distributed stain.

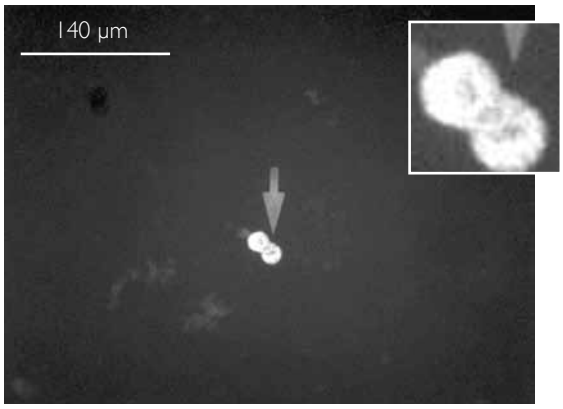


Figure 7: Basal cells stained for p-STAT3.
Nuclear&granular staining with difference between cells.

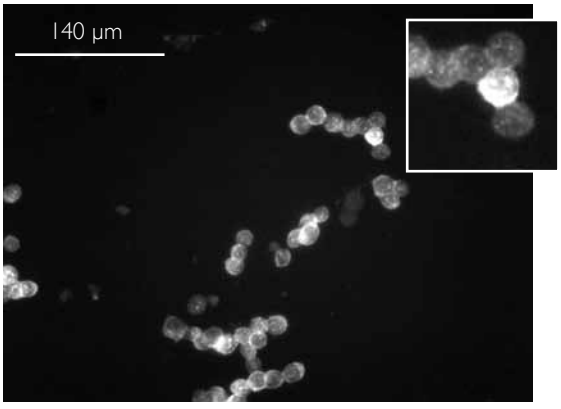
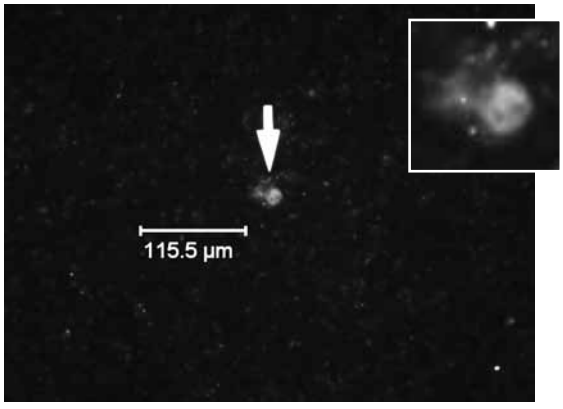


Figure 8: Prolactin-stimulated PC12 cell stained for p-STAT3.
The arrow points to a cell with stain mainly nucleus.



PC12 cell culture and transfection

PC12 cells were cultured with good adherence on 24-well plates containing collagen-coated cover-slips. Similarly, titrating the PC12 cells vigorously using a (0.5X25mm) needle gave a single cell suspension, which readily formed a monolayer distribution of cells when plated and thus reduced the lifting effect of non-adherent cells in larger clumps. PC12 cells transfected with the combination of 200ng/µl DNA and 0.35µl of Lipofectamine™ showed a few green fluorescent cells after 48h of transfection, indicating the incorporation of the p-EGFP-N2 vector into the cellular DNA (Figure 4). The cells that were not transfected were spherical and showed no signs of granulations indicative of Lipofectamine toxicity. Increased DNA concentration (500ng/µl) showed reduced transfection. The same was observed with reduced DNA concentration (100ng/µl). Longer duration of transfection showed no increase in the number of transfected cells; in that 72h transfection was similar to 48h. Cells grown in serum-containing medium for 24h prior to transfection were not transfected at higher rate compared with the cells grown in serum-free medium for 24h prior to transfection. Moreover, there were more cells transfected when the cells

were grown in 96-well plates compared to the larger wells in 24-well plates. This was consistent in three experiments.

mmuno-staining

Basal cells, grown in serum-containing medium with no PRL treatment, stained for STAT1 were strongly fluorescent. The stain was finely distributed in the cytoplasm but not the nucleus. There was a marked variation of brightness between groups of cells within the same well (Figure 5). In prolactin-stimulated cells, there was similar staining pattern to the basal cells but it may be less bright (Figure 6). Staining for p-STAT3 in the basal cells showed a different pattern compared to STAT1 staining. The stain was mainly nuclear and granular in nature. There was obvious variation in stain intensity between cells within the same well (Figure 7). PC12 cells that were stimulated with prolactin and stained for p-STAT3 were faintly stained but still with same staining distribution to the basal cells (Figure 8). The very low number of transfected cells resulted in no observable difference between transfected and non-transfected cells regarding prolactin response.

DISCUSSION

The increase in number of discrete colonies with increased bacterial amount indicates that there was a selection of transformed bacteria using neomycin containing dishes. Moreover, the control dish that did not grow any colonies ruled out contamination of neomycin resistance bacteria. Restriction enzymes, with their ability to cleave DNA sequences at specific sites, were a reliable test of identifying the presence of a specific DNA segment. According to the vector data sheet, the uncut vector is about 4.7kbp and that was confirmed in two sample of purified DNA. The region of the PRL dominant-negative receptor was demarcated by two combinations of restriction enzymes (EcoR1&BamH1/HindIII&BamH1) and they both gave two bands of the expected molecular weight of about 1kbp which represents the inserted construct and the 4.6kbp which is the carrying vector. The use of Xbal which has one recognition site gave similar picture to the uncut sample which means that cutting in one site only still create a one fragment of DNA. The restriction enzymes analysis confirmed that the purified DNA was the required construct. PC12 cells transfection in one study was reported to be about 14% efficient[5]. However, there were very few cells that were successfully transfected as indicated by GFP-fluorescence imaging. The observation of better transfection when the PC12 cells were deprived of serum-containing medium might be because serum contains biological molecules that interfere with the DNA/ Lipofectamine complexes. In addition, serum deprivation weakens cell membranes and facilitates the DNA/ Lipofectamine uptake[6]. For future projects, more easily transfected cell lines such as Chinese Hamner Ovary cells could be used. PC12 cells have been reported to respond to prolactin stimulation with a proliferative-type response[6]. This response is mediated mainly via the Jak2/ STAT pathway. In one study, STAT3 (p-STAT3) was measured using western blotting as marker for the PRL response in PC12 cells and demonstrated a significant increase after 15 minutes of stimulation[7,8]. In this project, immuno-staining for STAT1 and p-STAT3 was used as the measurement of PRL response. These were selected because STAT1 is mainly cytoplasmic and p-STAT3 mainly nuclear[8].

This project has demonstrated that there is a difference between the p-STAT3 and STAT1 staining. However, this difference could not be clearly related to prolactin stimulation. It was interesting to observe that basal cells stained more for STAT1 and p-STAT3 than prolactin-stimulated cells. At this moment, there are no clear explanations for this but questions of PC12 response to prolactin are still valid. In future research, it would be of great value to establish a cell line that is easily transfected with prolactin dominant negative receptors and are responsive for prolactin stimulation in a measured way. This will allow co-labelling and testing whether the dominant-negative receptor damps down the responsiveness of the cell line to prolactin. In general, it was valuable research project to address the difficulty that could be overcome next time in an attempt to understand the diverse functions of prolactin in biology.

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Global Health Conference 2009

Jasveen Kaur
4th year medical student
Wellington School of Medicine
University of Otago

Jasveen is a 4th year medical student in Wellington. She has attended several international conferences including two Global Health Conferences in Australia, and one IFMSA General Assembly in Mexico. Her passion for global health has inspired her involvement in NZMSA as sponsorship officer this year to explore ways in which global health groups can raise their profile amongst medical students in NZ.

From 2nd to 5th July 2009, I attended the Global Health Conference (GHC) in Brisbane, Australia. The GHC was run by the Australian Medical Students Association (AMSA) and held at the beautiful St Lucia Campus of the University of Queensland. I was only able to be there by the partial funding I received from the New Zealand Medical Association Leadership Fund. I would like to thank the NZMA for creating this opportunity for me.

What I found the most eye-opening at GHC were the talks on the realities of humanitarian field work. Problems of delivering aid were addressed. These included government resistance and corruption, lack of transport and infrastructure, communication difficulties, and the concept of teaching rather than bringing aid. Speakers provided possible solutions to these logistical and political problems which was great food for thought. They showed me how healthcare is one of the biggest political drivers in every country, and as doctors we cannot ignore social and political structure wherever we may go.

Other speakers addressed practical tips to aid work. In particular, Dr Nick Coatsworth, the Vice-President of Medecins Sans Frontiers (MSF) in Australia, spoke of the reality of being on the frontline in crisis areas. There were hard decisions to make about who to treat, when to leave, and what would happen when they left. In conjunction with this, "Triage" an emotionally charged documentary about the former International MSF President Dr James Orbinski was screened. It showed how ugly humanitarian work can be because of those hard decisions. I think aid work has been romanticised by a lot of enthusiastic young people, and it is necessary to see something like this to realise exactly how difficult a job it is. At the same time the documentary also showed the positive impact Dr Orbinski had on people he left behind in the Somalian famine and genocide in Rwanda. 'Triage' is definitely something I would encourage every medical student to watch before they graduate.

The "Challenge Day" consisted of a set of stations we rotated through in small groups. Each station illustrated a different aspect of global health addressed throughout the conference. Stations included carrying water in a standard issue 'developing country' bucket (a hole ridden bucket) from the beautiful University Queensland lake over 500 metres to illustrate what people in developing countries have to do everyday. Other stations addressed language barriers, resource allocation, emergency management, tropical diseases, and more. A lot of the "Challenge Day" was useful medically and could be something we could include in our student conferences here in New Zealand.

Overall I would recommend AMSA's GHC for every medical student interested in finding out how New Zealand doctors fit in with the rest of the world. The GHC is suited for all medical students at all stages of training because much of it is focused on thinking about the medical profession as a whole and how it fits into life.

Please don't hesitate to contact me or anyone else who has attended these conferences for more information.
jaska974@student.otago.ac.nz.

NZMSJ Features Writing Prize
Issue 10
FIRST PLACE

Lessons in humility on the Thai border

James Heaton
Bachelor of Medical Sciences
Deprtment of Medical and Surgical Sciences
University of Otago

James is a fourth year medical student at the University of Otago. With particular interest in research and medicine in developing countries, he aspires to one day work for organisations such as Medicins Sans Frontieres or the Red Cross. He is currently studying towards a BMedSci (Honours) at the Dunedin School of Medicine.

It took me a while but I eventually realised why I could not bring myself to enjoy the high life upon my return to Bangkok. I had just finished seven weeks as a volunteer research assistant at the Shoklo Malaria Research Unit (SRMU) in Mae Sot, a town in northwestern Thailand. Seven weeks earlier I would have killed to dine at the Hilton and drink the best whisky at the swankiest rooftop bar in downtown Bangkok. Those thoughts occurred however, before I had met my Karen colleagues in northwestern Thailand. I realise now that for the cost of my dinner, I could pay for the treatment of more than ten malaria patients, or feed a migrant family for more than two weeks[1].

The SMRU is a field station of the Mahidol-Oxford University Tropical Medicine Research Unit. Located on the Thai-Burmese border and established in 1986, SMRU specialises in the investigation and treatment of malaria and other tropical diseases. Working out of five clinics in the Tak province of Thailand, the SMRU has been a mainstay for the provision of medical care to tens of thousands of Karen refugees and migrants forced to flee Burma. The Karen people are the largest minority group in Burma, consisting of approximately 6-12% of the Burmese population of 47 million.[2-6] The Karen along with other ethnic minorities, have been fighting for an independent state since the end of colonialism in 1948, and still 60 years on, there is little sign of change.

In recent years the Burmese military junta's imposition of forced labour, land confiscation, agricultural production quotas and indiscriminate military operations against rebel groups and civilians alike has resulted in the displacement of over 500,000 people in Eastern Burma.[2,6] These people have been forced to hide in the jungles or cross the border into Thailand as refugees. It is this population, disowned by their own government, which the SMRU, along with other non-governmental agencies (NGOs), work to keep alive.

Of the half million displaced, approximately 135,000 are refugees.[2] These people place their lives in the hands of the Thailand Burma Border Consortium (TBBC), a cooperative of 12 NGOs providing everything from food and shelter to healthcare and education. These are the lucky ones. For the 400,000 other Internally Displaced People, life is a struggle for survival. Persecuted by their own government, they hide in jungle settlements where disease is rife and malnutrition is chronic. Many more thousands cross illegally into Thailand in search of work. Having fled their own country out of fear, a migrant worker has no rights and is forced to plead for illegal work in another. Employers know this and use it as leverage to exploit them. Migrant workers work long hours in return for meager pay. Within one kilometer of my guesthouse, there were two brothels and one factory employing almost exclusively illegal migrant workers. The black market is booming and the back pockets of policemen are very full.

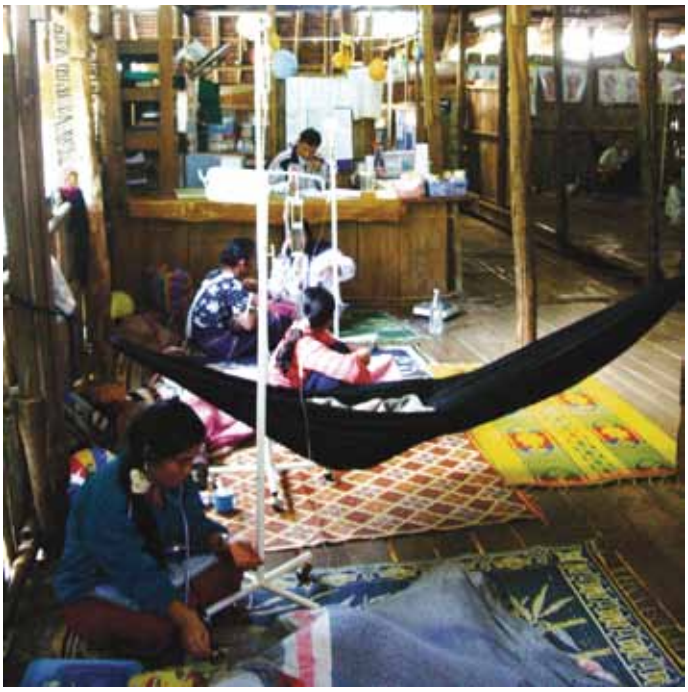
The length of the conflict has meant that the situation in the refugee camps differs from similar refugee situations around the globe. While still officially referred to as temporary shelters, many of the people in the camps have lived there for over 20 years. My peers at the camp are unlikely to have experienced life outside of the camp's four kilometres squared confines. Thankfully missionary schools offer some educational opportunities and my friends now hope that the United Nations High Commissioner for Refugees will arrange their resettlement in the United States, Australia, Europe or even New Zealand. The elders of the camp communities have given up on the dream of returning to a free Burma and instead work selflessly to provide hope and freedom for future generations.

The refugee camps are geographically beautiful, with bamboo and banana leaf huts surrounded by limestone cliffs and tropical forest. One might be forgiven for thinking they had found paradise. Upon closer inspection however, the camp is surrounded by armed checkpoints and barbed wire fences. The knowledge that clashes between freedom fighters and Burmese military are constantly occurring just a few kilometres away is unsettling.

Unable to leave the camps or even move freely within their camp, these people also have little chance to work. Refugees rely on handouts from NGOs. TBBC provides charcoal, oil, rice, beans and 'nya uti' (spicy fish paste, a staple in the Burmese diet) for each family and Aide Medicale International (AMI) and the SMRU provide health care.[3] AMI is able to manage and treat the majority of illnesses, from HIV through to fractures, while the SMRU specialises in malaria. The latter has had great success in eradicating most of the malaria within the camp and as such can now focus on tropical obstetric and paediatric care.

The SMRU provided me with an amazing experience in clinical medicine. Within my first day I had seen and palpated all the tell tale signs of malaria:

View across
Mae La refugee camp



In patient department at the Mae La clinic

spiking fever, chills and rigors, fatigue, weakness, anaemia, hepatomegaly, splenomegaly, and raised respiratory rate.[7] I was also able to examine blood smears with the mobile microscopy teams and learn to differentiate between strains of malaria parasite. Plasmodium falciparum and P. vivax predominated and I was quickly able to distinguish between P. falciparum's classical crescent-shaped gametocytes and P. vivax's ring-formed trophozoites.[7] Treatment options were limited, but specific protocols were in place to prevent parasite resistance developing. Every suspected case was investigated with a blood smear for typing and severity of malaria before treatment. P. falciparum is treated with a combination of mefloquine and artesunate, while P. vivax is treated with chloroquine.[7]

I was also privy to the cooperation between NGOs to optimize the health of the Karen people. Simple examples include giving them iodized rather than regular salt to prevent goitre; vitamin B1 supplements to prevent beriberi; and folate fortified flour. This along with education about health matters like HIV, TB, hepatitis and malaria prevention are multi NGO cooperative initiatives, which greatly improve the wellbeing of the refugees.

Exposure to the inner workings of an NGO providing care to a dependent population also opened my eyes to many other aspects of human care. The SMRU has to constantly produce top grade research in order to receive continued funding. Many of the doctors live and breathe their work to achieve this and ensure continued treatment for their patients. One research project I worked on was assessing crowding within the refugee camp. This gave me the privilege to move through the camp and into the homes of refugees. I was able to see the minimalistic living conditions of the refugees. Families, often with more than ten members, live in huts smaller than the size of a bedroom; and a mere flat bamboo wall separates them from the next family. There is no such thing as privacy in the camps. No-one complains. They appear to be happy as they are safe and their basic needs are being met.

It was this exposure to a community without possessions that had the biggest effect on me. Each person in the camp was living in a borrowed hut, off donated food, and cooked with donated charcoal on a borrowed clay stove. Their humility was admirable. Money was non-existent and the simplest of pleasures sufficed. I was repeatedly humbled by the sight of children shrieking with delight, while they played with dusty wrinkled balloons that I had handed out days before.

As we become doctors we learn of ways to gain the trust of our patients so that we may assist with their health. The refugees and displaced migrants have no option but to trust others for their survival. Choice is no longer an option in regards to the availability of different types of food, treatment options, or midwife to oversee the birth of an expectant child. As a third

Checkers outside Mae La clinic. Rocks vs pebbles

year medical student this was very disconcerting. Coming from the New Zealand medical environment, where students know enough to know they know very little, I initially had little confidence in my own ability to provide the refugees with adequate medical care. Yet mothers would readily entrust me with their children for examination. Having been exposed to the lives of the Karen people, I am astounded they can trust anyone. Being trusted to give care made me realise that this was something I could do on a basic level. This was a perfect confidence boost prior to beginning my clinical years.

The Karen people are in a unique and unenviable situation with no easy solution. Nonetheless I will always remember their optimism. For me, the chance to live, work and learn from them was a priceless gift. They showed me that happiness doesn't come from anything we can buy in a shop. It comes from the people around us and the relationships we forge.

You will have noted that I did not refer to Burma as Myanmar. I urge you to do the same. This is at the wishes of my Burmese colleagues. The Union of Myanmar is the term introduced by the SPDC, the State Peace and Development Council. Refusal to acknowledge this term is in protest of the multitude of state sanctioned human rights abuses committed throughout their rule.

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Fiji Village Project;
Treating the patient, the water or the village?

Carolyn Deng
Trainee Intern
School of Medicine
University of Auckland

Carolyn Deng is currently a trainee intern (MBChB VI) from the University of Auckland. Her involvement with the Fiji Village Project began in 2007 with the first project cycle. She is the NZ coordinator for the project this year. She will be working as a first year house officer in Auckland DHB next year and aspire to train in medicine and complete a Masters in Public Health in the future.

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In 2005 the World Health Organisation estimated that 1.1 billion people lack access to safe drinking water. A total of 2.6 billion people, 42% of the world's population, lack access to basic sanitation.[1] It is tempting to dismiss these statistics to areas such as Africa and South Asia, but the reality is that even our neighbouring Pacific Islands suffer severe and chronic water stress. In 2004, the Pacific Institute estimated that only 47% of the population of Fiji had access to safe drinking water, a massive decrease when compared to 1994, when almost 100% of both the rural and urban populations had access to safe water.[2] Diseases related to poor water and sanitation such as dengue fever, leptospirosis, typhoid, chronic diarrhoea and infective skin conditions are rife in both the rural and urban parts of Fiji and it is not difficult to see why.[3]

The lack of a safe water supply clearly has a huge impact on health, but also perpetuates gender inequality, loss of schooling or working time, and social insecurity. This leads to a vicious cycle of sustained poverty and slow economic growth. Issues with water supply go hand in hand with basic sanitary measures. The mass dumping of household and industrial sewage and waste into water courses, particularly in developing countries, is responsible for polluting the already scarce water supply.

The Fiji Village Project, an international student-led humanitarian project, was started in 2007 by medical students across Australia, New Zealand and Fiji to address basic public health deficiencies such as water sanitation. The New Zealand branch of the Fiji Village Project also works in partnership with Medical Students for Global Awareness, a student organisation that promotes social responsibility and awareness of global issues.

The new water tank for Ro Camaisala Memorial School.

Tanya (an Australian medical student) checking the BP of one of the villagers as part of health screening.

Students from Ro Camaisala Memorial School in Nabukavesi, participate in an educational programme facilitated through art and music.

The Fiji Village Project is a year-long commitment ending with an annual two week project trip to Fiji in mid to late January. The last two project cycles in January 2008 and 2009, although not solely concerned with water sanitation, have focused largely on the provision of rainwater harvesting tanks to two villages near Suva: Nabukavesi and Qilai. This focus works towards one of the UN's Millennium Development Goals, "to halve, by 2015, the proportion of the population without sustainable access to safe drinking water and basic sanitation".[4] The United Nation's International Decade of Action Water for Life runs from 2005 to 2015 and generated much motivation for the project to address these water, sanitation and hygiene issues.

The first project cycle in January 2008 worked with Nabukavesi, a village with a population of 600, situated 8km from Suva central. The only water supply to the villagers was an old dam with a capacity to supply water for 100 individuals. Through fundraising and sponsorship events, enough money was raised for the project to install three rain water tanks for the local primary school in Nabukavesi. Prior to this, the dam closed down twice a week due to water shortages and impacted immensely on the education of young children in Nabukavesi. A similar approach was taken with the village of Qilai in our second project cycle with funds used for enlarging their existing local dam and installing water tanks for clean drinking water. Health screening for hypertension, obesity and diabetes were also held as part of both trips, with coverage rates 70-90% of the village population. Educational programmes on basic public health measures were held and these focused on achieving a healthy lifestyle, safe sex, water sanitation, and promoted screening programmes such as cervical smears. We are currently undergoing preparations for our third project cycle in 2010 which will have similar goals as our two previous projects.

The Fiji Village Project not only provides aid for those who are less fortunate than us, it also serves as a reminder to all those involved that there are reasons behind each illness and that the key to health is not as simple as treating the patient as an entity divorced from his or her beliefs, family, village or governmental policy. As future health professionals, we must prepare ourselves for the immense power granted to us by the nature of our work. No other profession allows us to interact so intimately with strangers we have met just moments ago. Perhaps we can create change in a patient's life or in the society of a patient that will reduce his chances of falling sick in the future. Surely by now you are sick of hearing analogies containing cliffs, ambulances and bottoms. As health promoters, we must treat both the well and the sick. Professor Fran Baum, a Commissioner on the WHO's Commission of the Social Determinants of Health once said, 'It does no good to heal people's illnesses but send them back to the conditions that originally made them sick' (A. Talemaitoga, personal communication, 2009).

The Fiji Village Project has a public health focus and allows students to address some of the most difficult health issues in a rural village and devise solutions that are both sustainable and feasible under resource constraints. It is clearly a small beginning to the immense need of the world in order to achieve the Millennium Development Goals by 2015. Can we afford to help in the midst of this great recession? A WHO cost-benefit analysis estimated that every US dollar spent on improving water and sanitation

Paul Shotbolt (MBCHB 3) participating in a village education session on HIV and AIDs.

yields an economic benefit of $4 to $34 depending on the region. The US$11.3 billion per year needed to achieve the Millennium Development Goals will yield US$84 billion in economic development.[1] The question is not whether we can afford to help, but whether we can afford not to.

The Fiji Village Project is an initiative that can be embraced by all those in the health profession, and the project would not run successfully if not for the support of all our sponsors and students across both the Auckland and Otago campuses. Fiji Village Project is a grassroots organisation and as such needs the collective support of the student body. Although a small-scaled project, the Fiji Village Project perhaps gives a glimpse to the big things that we as students can achieve for the world if we stand united in our vision for a better future.

How to contribute:
To donate to the Fiji Village Project, contact Olivia Perelini (Treasurer) at liv_perelini@hotmail.com or Carolyn Deng at carolyn.deng@yahoo.com

More projects around global development?
Global Poverty Project –
Contact Divya Dhar at divya.dhar@gmail.com
Medical Students for Global Awareness –
Contact Sudhvir Singh at sudhvir@hotmail.com

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The Digital Rectal Examination – more than assessment of the prostate gland

Siddiqui MRS
Surgical Specialist Research Registrar
Worthing Hospital
West Sussex, United Kingdom

Sajid MS
Surgical Specialist Registrar
Worthing Hospital
West Sussex, United Kingdom

Azeez A
Medical ST1
Aintree Hospital
Liverpool, United Kingdom

Baig MK
Consultant General Surgeon
Worthing Hospital
Worthing, United Kingdom

Muhammed Siddiqui is currently a surgical registrar at Worthing Hospital, UK. He studied at the University of Liverpool and had an interest in general surgery at an early stage of his career. He has a keen interest in teaching and is currently doing a Masters in Medical Education. As a medical student he used to learn a whole heap of facts and things to do during clinical examinations without really knowing what he was looking for. He hopes that his short article provides you with a framework for performing a digital rectal examination.

ABSTRACT

The digital rectal examination (DRE) is a fundamental part of the abdominal examination. Its technique is explained and taught well in medical schools and its importance is highlighted. I recently asked my house officer to perform one and was surprised by their lack of understanding as to what they were looking for and the reasons for performing it. It concerned me that perhaps there were other junior colleagues who did not fully appreciate the reasoning and were therefore not obtaining adequate or appropriate consent prior to the examination. This article sets out a framework for performing a DRE and the implications of the common findings. I hope that this article will subsequently be used by future junior doctors to obtain informed consent according to Medical Council guidelines.

INTRODUCTION

You complete a beautiful abdominal examination and get ready to present to your educational supervisor. As you get to the end of the presentation you remember to tell him that you would always perform a digital rectal examination (DRE).[1]

Your supervisor congratulates you on remembering an extremely important feature of the exam. The conversation proceeds to asking why it is important.

You manage to stutter out a couple of answers like assessing the prostate gland and whether there is hard stool in the rectum or not.

You receive congratulations again and your beleaguered brain lets out a sigh. Your consultant then asks you 'what else?'

Indications

Junior doctors are required to give patients information on the need for aspects of examination, investigation and treatment.[2] The DRE is important in the assessment of the anorectal region, the prostate gland in men, the cervix in women, as well as manual bowel evacuation.[2] Every patient should have a digital rectal examination except in certain circumstances, for example in children, those who do not give consent, conditions such as acute epididymitis, and in those patients where a rectal examination is not going to affect your management[3-5]; particularly if the patient is likely to be referred to a specialist where a repeated examination will take place.[6]

The key is classification

Medicine is all about classification and applies both to academic and clinical skills. Academic medicine has its own classifications depending on the particular topic one looks at. Clinical skills have traditionally been classified into Inspection, Palpation, Percussion and Auscultation. These four aspects are based upon the senses which all doctors possess.

Often in clinical practice the sense of touch is the only one that is used when performing a DRE. This article aims to describe the DRE in terms of the five senses (sight, smell, touch, hearing and taste) and the stage of the examination (at the beginning, middle, and end).

How to perform a digital rectal examination

This article describes one way of performing DRE practised in our department.[7] Stress must be given to the importance of informed consent along with a chaperone.

Consent

Informed consent is important; merely explaining that you need to do the procedure as part of a complete examination is inadequate. Imagine you are the patient and someone who you do not know wants to place a finger in your anorectal canal. I know that if I was in hospital, I would want a good reason for it. Furthermore as a clinician you should want a pretty good reason for doing it yourself.

One should also be aware that there are a number of reasons that patients refuse an examination ranging from fear of finding a cancer to discomfort and embarrassment.[8] These concerns should be addressed as appropriate with adequate explanation and offering someone of the same gender to carry out the procedure although this may not always be of concern to the patient.[9]

The findings outlined below are the commonest reasons for performing a DRE examination and should be used in attaining informed consent.

The Procedure

After appropriate consent and preparation, the patient is positioned on their left side with the knees and hips flexed so that the knees are pulled towards the chest (Fig 1). The buttocks should be close to the edge of the bed.

A gloved finger lubricated with KY jelly should be inserted into the anal canal and after completion the finger withdrawn. The patient's anus should be wiped afterwards and the patient thanked for their patience.

Figure 1. Positioning the patient in preparation for the examination.

Figure 2. Inserting the finger.

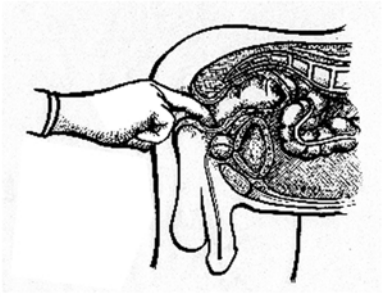

Figure 3. The anal canal and recum as a garden shed with five sides and an opening.

In The Beginning

The positioning of the patient will indicate a lot.

Is the condition causing them pain?

If the patient is elderly can they get into the correct position easily? If they struggle it may mean initiating the request for social services earlier rather than later.

On the left lateral side

What do you see?

- Is there discolouration around the anus?
  - Remember the bluish tinge around the anus for Crohns?
  - Is there erythema?
    - » Is there an underlying abscess?
    - » Is there persistent diarrhoea or incontinence causing irritation?
- Are there any prolapsed haemorrhoids?
- Is there a skin tag which may or may not be bleeding?
- Is there a swelling?
  - Is there pus, or is there pointing on the surface?
  - Is there an irregular swelling/mass suggestive of an anal cancer?
- Are there any signs of an operation?
  - Scar tissue
  - Discharging pus (do they have a fistula?)
  - Do they have a Seton in the fistula?

Inserting the finger

As you place your finger at the edge of the anal opening, about to insert your finger in (Fig 2)

What do you hear from the patient?

- Is it painful?
  - Indicating an underlying collection or irritation eg diarrhoea
- Is it painless?
  - Is there a spinal cord lesion if they can not feel you?

What do you feel?

- Does the skin around the anus feel thickened and indurated
  - Indicative of an underlying collection of pus
  - Is it cellulitis?

As you insert your finger

What do you hear from the patient?

- Is it painful
  - Could there be an anal fissure?

When completely inserting your finger, the anal canal and rectum can be considered as a garden shed with 5 sides and an opening (Fig 3).

What do you feel and hear from the patient?

At the 3 o'clock surface

In a man:

What does the prostate feel like?

- Could it be enlarged due to benign prostatic hypertrophy?
- Could it be a prostate cancer if it feels irregular?

Is the prostate tender?

- Could he have acute prostatitis?

Is it flattened?

- Indicative of previous surgery
- Has he had a TURP?

In a woman:

Is the cervix tender?

- Is it pelvic inflammatory disease?

At the 12 o'clock surface

Are there any masses?

- Any hard mass is cancer until proven otherwise.

Is it tender?

- Could there be a pelvic collection?
- Could there be a low lying appendicitis?

At the 6 and 9 o'clock surfaces

Is it tender?

- Is there a collection?

Are there any masses?

The roof (of the shed)

Are there faeces?

- Can you break it up or is it completely impacted?

Removing the finger

What do you see?

- Stool
  - What colour is it?
    - » Do they have obstruction?
    - » Do they have jaundice and biliary disease?
  - What is the consistency?
    - » Are they just constipated?
    - » If loose and sloppy do they have an enteritis?
- Blood?
  - Fresh – Could there be an anal fissure or haemorrhoids?
  - Dark – Do they take iron?
  - Mixed with stool? Is there a pathology higher up like inflammatory bowel disease or diverticular disease?
  - Black – is there an upper GI bleed?
  - Mucous/ Slime
    - » Do they have a polyp secreting mucus?

What do you smell?

- Is it pungent and sweet?
  - Is there an upper GI bleed?

The above method uses four senses in a chronological way when performing a DRE. The omitted sense is taste, but since smell is a large constituent of taste, you should remember that the next time you smell a maleana you are experiencing the taste as well!

CONCLUSION

The above findings for each of the senses are not intended to be exhaustive, but highlight the questions and answers that can arise from using all your senses when performing a DRE. Combined with an adequate history it can clinch a diagnosis, avoiding unnecessary, expensive tests and investigations, or indeed leading to more appropriate investigations. Furthermore I hope the classification above provides some insight into exactly why a DRE is so important and may help in informed consent when performing one on a patient.

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NZMSJ Academic Writing Prize
Issue 10
SECOND PLACE

Hypomania: A brief review of conceptual and diagnostic issues

Thomas Hugh Richardson
Research assistant
Mental Health Research and Development Unit
University of Bath, England

Thomas Hugh Richardson completed his undergraduate Psychology degree at Trinity College Dublin, Ireland, graduating with a first class honours in 2008. The paper submitted is based on a literature review undertaken as part of his final year dissertation research project entitled: "Hypomania: epidemiology and relationships with substance abuse, impulsivity and risk-taking behaviours". Thomas has worked widely in the area of mental health, working with a range of mental illnesses. Thomas has also been involved in a number of research projects, and is currently working as a research assistant at the University of Bath, England, investigating CBT based computer programs to help with depression and anxiety in adolescents. Thomas now lives in south west England where he grew up, and intends to study to become a clinical psychologist in the U.K. National Health Service.

Historical descriptions

Ideas of hypomania have existed for over 2000 years[1], while Hippocrates formed concepts of mania in the 5th century BC. In the 1st century, the Greek physician Aretaues classed 'mania' and 'melancholia' as two opposites on a spectrum of the same disease[1]. However, modern concepts of such a spectrum as representing 'bipolar disorder' did not arise until much later. This concept was studied in the 19th century when Falret in 1854 and Hecker in 1898 described the symptoms of hypomania in detail[2,3]. The term 'hypomania' was first used by Mendel in 1881[4], followed by a classic description by Kraepelin a decade later, who introduced the term 'Manic Depression' in his book published in 1921[5]. Also in 1921, Kretschmer described the premorbid personality features of those who develop bipolar disorder[6]. The term 'bipolar disorder' was first used by Karl Leonhard in 1957[7], but this was not introduced as a diagnosis until 1980. Despite the early descriptions of hypomania, there are still a number of diagnostic controversies in the area, and this is reflected in the differences between the two most common diagnostic systems, ICD-10 and DSM-IV-TR.

Hypomania: symptoms and diagnoses

As Figure 1 demonstrates, according to the DSM-IV-TR, a 'hypomanic episode' is a mental illness characterised by symptoms such as flight of ideas, a decreased need for sleep, elation, grandiosity, talkativeness, and an increase in goal-directed activity. These symptoms occur within an elevated or irritable mood which lasts at least 4 days. This mood and behaviour is different from the way the person normally behaves, which is obvious to others. These effects do not cause significant impairment in social or occupational functioning, and are not directly due to physiological mechanisms. Multiple hypomanic episodes with multiple episodes of major depression leads to a diagnosis of bipolar II disorder, whereas multiple manic episodes often with multiple episodes of major depression leads to a diagnosis of bipolar I disorder. If an individual frequently fluctuates between hypomanic and depressive symptoms then a diagnosis of cyclothymic disorder is appropriate. Thus it is necessary to examine full history of both depressive and manic/hypomanic symptoms of a patient to deduce appropriate diagnosis.

There are a number of similarities between the DSM-IV-TR and ICD-10 criteria. For example, the ICD-10 also describes elation of mood, talkativeness and irritability as key symptoms. Additionally, both the ICD-10 and DSM-IV-TR hold that psychotic symptoms such as hallucinations and delusions cannot be present. However, there are a number of differences in the criteria, for example the ICD-10 does not place emphasis on the duration of hypomania as part of diagnostic criteria. This is in line with research demonstrating that this criterion is unnecessary as an accurate diagnosis can be made without taking into account duration[8], and the majority of hypomanic episodes occur for less than 4 days[9].

Mania-Hypomania Distinction

The distinction between mania and hypomania is poorly defined, complicating diagnosis. However, this distinction is important as depression with hypomanic episodes will lead to a diagnosis of bipolar II, whilst depression with mania leads to a diagnosis of bipolar I disorder. Both disorders have different prognoses, and require different treatment[1]. Thus clear diagnostic criteria are needed, but are often indistinct. This occurs in research, and also clinical practice[10]. The DSM-IV-TR criteria are virtually identical, characterising hypomania as a lesser degree of manic intensity than mania. Therefore the diagnostic distinction between the two is that a hypomanic episode is not severe enough to cause marked impairment in social or occupational functioning, or to require hospitalisation, and that there are no psychotic features[7]. The ICD-10 takes a similar stance in terms of differentiating the two by emphasising that any "Severe or complete" negative impact on functioning would differentiate the two, though the ICD-10 does suggest that "considerable interference" is possible in hypomania[11,12]. However the key difference is that the ICD-10 essentially describes hypomania as a more severe mental illness than the DSM-IV-TR. As a result, ICD-10 essentially lowers the threshold between hypomania and mania. As Goodwin[10] puts it; "In ICD-10 hypomania is an almost superfluous term that describes mild mania, whereas DSM-IV offers us something different".

Many of these diagnostic distinctions between hypomania and mania have been challenged. For example, whilst a number of authors have found that hospitalisation distinguishes the two[13], it could be argued that hospitalisation is an artificial and meaningless criterion, as this may depend on irrelevant factors such as number of beds available. Also, it is generally

Figure 1: DSM-IV-TR criteria for a Hypomanic Episode

DSM-IV-TR criteria for a Hypomanic Episode

A. Distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 4 days, that is clearly different from the usual nondepressed mood.

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

(1) Inflated self-esteem or grandiosity

(2) Decreased need for sleep (e.g. feels rested after 3 hours of sleep)

(3) More talkative than usual or pressure to keep talking

(4) Flight of ides or subjective experience that thoughts are racing

(5) Distractibility (i.e., attention, too easily drawn to unimportant or irrelevant external stimuli)

(6) Increase in goal-directed activity (either socially, at work or school, or sexually, or psychomotor agitation)

(7) Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

C. The episode is associated with an unequivocal; change in functioning that is characteristics of the person when not symptomatic.

D. The disturbance in mood and the change in functioning are observable to others.

E. The episode is not severe enough to cause marked impairment in social or occupational functioning, or to necessitate hospitalisation, and there are no psychotic features.

F. The symptoms are not related to the direct physiological effects of a substance (e.g., a substance, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

accepted that psychosis and the consequential negative effects on social or occupational functioning only occurs in mania, though this is controversial, as there is evidence to link hypomanic episodes with significant negative consequences[14], as will be discussed in greater detail later. Whilst flight of ideas is held to be present in both hypomania and mania, flight of ideas is less frequent in hypomania than mania, and such thinking patterns vary considerably between the two[15]. The concept that hypomania is essentially a milder form of mania is also controversial, as hypomanic symptoms frequently fail to present in the way assumed by diagnostic criteria which are developed from the criteria for manic episodes[16]. Whilst the DSM-IV, and to an extent the ICD-10, assume that the symptoms are the same, factor analysis suggests there may be differences both in the prevalence of specific symptoms and their clusters in hypomania and mania[17,18,19]. Evidence from a number of lines of evidence suggests that hypomania is more than simply a less severe form of mania.

However, many of the diagnostic distinctions between hypomania and mania have proved to be correct. Kessing[20] found that mania was associated with a longer hospitalisation than hypomania. Other research has shown that hypomania rarely requires hospitalization[13]. Also there is clear a relationship between mania and hypomania. Whilst mania is associated with a longer recovery, hypomania and mania have the same risk of relapse[20]. Both hypomania and mania can present with depressive symptoms, leading to the diagnosis of a mixed episode. The risk of hypomania ultimately increases the risk of mania, as 5-15% of individuals with hypomania will ultimately develop a manic episode[12], and those with bipolar I disorder

Figure 2: ICD-10 criteria for Hypomania

ICD-10 criteria for Hypomania

A disorder characterized by a persistent mild elevation of mood, increased energy and activity, and usually marked feelings of well-being and both physical and mental efficiency. Increased sociability, talkativeness, over-familiarity, increased sexual energy, and a decreased need for sleep are often present but not to the extent that they lead to severe disruption of work or result in social rejection. Irritability, conceit, and boorish behaviour may take the place of the more usual euphoric sociability. The disturbances of mood and behaviour are not accompanied by hallucinations or delusions.

will cycle between euthymia, hypomania and mania during the course of their illness. Despite the general consensus that mania is associated with more psychotic features than hypomania, a greater risk of hospitalisation and more negative consequences, clearer differentiation between the two may be necessary for DSM-V and ICD-11. These differences between hypomania and mania are important for clinicians to consider, in order to ensure accurate differential diagnosis and subsequent effective treatment.

Does 'unipolar hypomania' exist?

An understudied area in bipolar disorder is the possibility of unipolar hypomania or mania, where one would meet the diagnostic criteria for episodes of mania or hypomania, but not depression. A DSM-IV-TR diagnosis of Bipolar II disorder assumes the presence of depressive episodes, and the criteria for bipolar I disorder states that depressive episodes often accompany manic episodes. Those with hypomania but not depression can be placed in the Bipolar Disorder Not Otherwise Specified category[12]. Klerman[21] found evidence to support the concept of unipolar mania, and Soloman et al[22] found that 18.5% of patients over a 20 year period initially diagnosed as suffering from a manic episode did not suffer from depression, further supporting the notion of unipolar mania. The only estimate of a population prevalence of unipolar hypomania was Angst et al[23] who found that, over 20 years, 3.3% suffered 'pure hypomania', and 0.97% of the population manifested hypomanic symptoms without qualifying for a diagnosis of any form of depression. However, this area is still greatly understudied, with the only epidemiological research on the area being conducted within the population of Zurich, Switzerland. It is important to consider the possibility that those presenting with hypomanic symptoms may not suffer from depressive episodes, and thus may not meet the full DSM-IV-TR criteria for bipolar II disorder. Such a possibility is addressed by the ICD-10, which includes the potential diagnosis of 'Bipolar affective disorder- current episode hypomanic', where previous episodes necessary for such a diagnosis can be hypomanic, manic, depressed or mixed.

The 'broad spectrum' of bipolar disorders

Some in the academic community have evolved from a categorical to a continuum conceptualisation of bipolar disorders. Taylor & Abrams[24] were the first to urge for a broader concept of bipolar disorder. As a result the concept of a 'soft bipolar spectrum' developed[25] which goes beyond descriptions of classic mania, and broadens the definitions of bipolar II disorder to incorporate depression with mild hypomanic episodes. The DSM-IV and ICD-10 categorical classification has been criticised, with individuals arguing that bipolar symptoms are present in a continuum within the general population, and that there is a spectrum of manic conditions going from classical psychotic mania through to sub-clinical forms of hypomania[21]. The Zurich study[26] supports this spectrum concept, showing that hypomanic symptoms are highly prevalent in varying degrees throughout the population. The Zurich study also developed its own 'strict' and 'broad' criteria for hypomania which have been applied to research[27].

Additionally, there is evidence to suggest that a broad bipolar spectrum is also present in clinical populations[28]. More recently, Akiskal and Akiskal[29] has noted that melancholic depression has many of the same risk factors as hypomania, and argued that melancholia should become part of the bipolar spectrum. Akiskal and Akiskal[29] argue that melancholia often represents a mixed bipolar state, and it is often associated with varying dimensions of hypomania and psychosis. Akiskal and Benazzi[30] found evidence which they claim suggests that both DSM-IV-TR and ICD-10 classifications of unipolar and bipolar disorder lie on a spectrum, and thus categorical distinctions between the two may not be valid. Another relevant concept is the notion of a 'hypomanic personality', where individuals are energetic, emotional, overly confident, extraverted, impulsive and ambitious[31]. Such a personality has been shown to be predictive of bipolar disorder up to 13 years later[32]. This concept of a bipolar spectrum suggests that such symptoms have a wide distribution within the general population. There has been little epidemiological research into such soft bipolar conditions, nevertheless it is important for clinicians to understand that as hypomanic symptoms are present on a continuum, the diagnostic threshold for hypomania may be essentially arbitrary and somewhat subjective. Thus it is important to consider the possibility of a threshold effect - a small number of additional symptoms may lead to a positive or negative diagnosis of bipolar disorder. However, once diagnostic critieria are met, any symptoms beyond this are not taken into account. As a result, a number of authors have suggested that the DSM-V and ICD-11 need to include dimensions into the diagnostic criteria for bipolar disorder so that specific symptoms are scored on a scale of severity[33].

Positive and Negative consequences of hypomania

Unlike mania, the DSM-IV-TR states that hypomania, is not associated with significant deterioration of functioning[12]. Similarly the ICD-10 holds that mania is associated with greater disruption than hypomania. However, a body of research has examined the effects of hypomania on the individual, discovering negative effects of such behaviours. In adolescents, hypomanic episodes are associated with antisocial behaviour, drug use and truancy[12]. Akiskal & Pinto[34] conducted a factor analysis of hypomanic symptoms, finding what they term the 'dark side' of hypomania. This included variables such as irritability, impatience, increased sex drive, excessive spending, and increased consumption of alcohol, cigarettes and coffee. Hypomanic symptoms have been found to increase lifetime health service usage, need for social welfare and disability benefits, and elevate suicidal risk[14]. Hypomania is also related to marital disruption, with the divorce rate being 6 times higher in hypomanics compared to controls[26]. Hypomanic individuals often receive very negative comments from those close to them about their behaviour, but can be oblivious to this[35]. Thus there is evidence to suggest the need to revise the DSM-IV-TR diagnostic criteria with regards to negative consequences may need revision, and perhaps should be brought in line with ICD-10 criteria which allows for mild but not severe disruption of functioning. Subsequently it is important to note that hypomania can lead to negative consequences if not treated rapidly and effectively.

Research has suggested occasional positive consequences to hypomanic behaviours. Akiskal & Pinto's[33] factor analysis also found evidence for a 'sunny side' of hypomanic symptoms, including socially positive and advantageous effects such as more drive and energy, increased social activity, increased talkativeness and more likely to laugh. There is often improved functioning associated with hypomania[36], including socially desirable symptoms, and increased charisma and leadership skills[37]. It has been argued that hypomania is in fact adaptive[38]. John Gartner in his book "The hypomanic edge; the link between a little craziness and a lot of success in America" reviews the histories of a number of important figures in American history, finding that they display increased hypomanic symptoms[39], supporting the argument that there are benefits to a hypomanic temperament. This is important for clinicians to consider, as the positive symptoms sometimes linked to hypomania may mean that patients are reluctant to seek treatment and adhere to a treatment regimen, and families and friends may find it harder to recognise these 'positive' symptoms as part of a clinical condition.

CONCLUSION

In conclusion, despite hypomania being described for hundreds of years, a number of diagnostic and conceptual issues remain, with differing conceptualisations in the DSM-IV-TR and ICD-10 comparatively. The symptoms and related diagnoses are often controversial; in particular what distinguishes mania from hypomania, and whether such a diagnostic distinction is in fact valid. A related point is whether hypomania always occurs as a part of bipolar II disorder, occurring with recurrent depressive episodes, or whether individuals can be a 'unipolar hypomanic'. Whether hypomania and related bipolar disorders should be classed categorically or on a continuum is controversial, and is limited by the lack of epidemiological research within the general population in this area. Finally, the positive versus negative consequences of hypomania are disputable, in particular because diagnostic criteria assume that such negative consequences are rarely associated with hypomania. These issues need to be taken into account by clinicians to inform effective diagnosis and treatment of hypomania, and also to help guide future research. Such diagnostic difficulties will be particularly important during the construction of the DSM-V and ICD-11 which are currently under way.

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Soft drink tax: an ideal solution?

Rebekah Jaung
4th Year Medical Student
University of Auckland

Rebekah is currently a 4th year at Auckland. Her medical interests include: General Surgery and Endocrinology. In her spare time she enjoys reading subversive socialist literature and baking.

The taxation of sugared beverages has become a topical issue in recent years. It has been proposed that this good should be taxed in a similar manner to alcohol and tobacco products with the purpose of improving healthcare and generating revenue for the government. This commentary will look at some of the issues that soft drink taxation and other 'sin taxes' may have on those of low socioeconomic status.

The predicted outcomes of such a 'sin tax' were discussed in a recent piece in the New England Journal of Medicine.[1] The rationale behind the proposed tax is that overconsumption of soft drinks is a contributor to obesity and related conditions, such as type 2 diabetes mellitus and vascular diseases. By implementing a tax, it is hoped that consumption will decrease. Additionally, revenue generated from the taxes can be channelled into improving other health services.

One interesting aspect mentioned by Brownell et al. was that those of low socioeconomic status would derive the greatest benefit from the proposed taxation framework. It is reasoned that this group carries most of the health burden of high calorie diets at present and would be most affected by the higher cost of such products.[1]

However, such a tax may have a disproportionate effect on the quality of life of low socioeconomic individuals. It has already been established that fat and sugar make up a higher proportion of the dietary intake for lower income households compared to higher income households, largely because consumers consider them to be the cheapest source of dietary energy.[2] Taxation of soft drinks may play a part in increasing the difficulty for lower income households to maximise their food budget in terms of energy density. There has been research conducted which shows that buying healthier products does not incur a significant added cost[3]; an important message currently being highlighted by public education campaigns. As of yet, it is unclear how much impact these campaigns are having, therefore developing other methods of improving nutrition and decreasing the number of overweight and obese individuals are still important.

Apart from economic considerations, the suggestion of soft drink taxation also raises social issues. Food is much more than merely a source of energy. It is a central component of a person's culture and perceived quality of life. In this respect, food preference may be more significant for those who can afford few luxuries. This issue was explored by Orwell in 'The Road to Wigan Pier'.[4] He commented, "the less money you have, the less inclined you feel to spend it on wholesome food … when you are underfed, harassed, bored and miserable, you don't want dull wholesome food."[4] He reasons that individuals of lower social economic status are the major consumers of highly processed, high calorie foods, as it is one of the cheapest sources of enjoyment available to them. If prices of such goods were raised, these pleasures could be taken away from the people who appreciate it the most.

Orwell goes on to argue that while the negative outcomes of a life in poverty are bad, using inhumane and degrading tactics to change these situations may also be of questionable value: "Bugs are bad, but a state of affairs in which men will allow themselves to be dipped like sheep is worse."[4] The aim of reducing disease by decreasing soft drink consumption is commendable but in terms of achieving wider health equality, restricting a decision as personal as food choice may be a misguided effort. If an individual does not feel that they are being treated with respect and equity, it is easy to imagine that their quality of life will suffer.

In addition, this issue may also be cause for us to reflect on our own perspectives on 'sin taxes' and the reasons and possible biases behind them. Orwell comments that if we as a society limit a person to poverty, it is even more disrespectful for us to tell them how to spend their money.[4] Although there may be disagreement with regards to the degree to which society impacts on those in poverty, it is clear how our efforts to 'improve the lives' of these individuals may seem impertinent, especially to the people in question. This brings to the surface questions regarding biases based on socioeconomic status with which we must deal with in order to truly have our patients' best interests in mind.

Some may argue that these social issues are not a concern of health professionals, and that the benefits of taxation far outweigh any disagreeable social implications. However, achieving equity is beneficial to the health of an individual and should be taken into account within reason. As future health professionals and advocates, we have a responsibility to do our part in making a patient's healthcare as empowering and fair as we can. Furthermore, as those fortunate enough to have the opportunity to attain a higher level of education and standard of living than many of those around us, we should not assume we have the authority to regulate all areas of other people's lives. A soft drink tax may well be the best strategy for improving the current outlook for obesity and related illnesses; however, if and when such policies come into place, we must be aware that they may have an impact on patients beyond counting calories and the immediate health burden. Ideally, as future advocates for health, we should look further than mortality and morbidity to changing the structure of the society in which we live. Ultimately it is the only way to correct health problems caused by societal inequality.

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Tom Hills
Trainee Intern
Wellington School of Medicine
University of Otago

Tom Hills is a Trainee Intern at the University of Otago, Wellington School of Medicine. His main interests are outdoors - running, cricket, surfing etc. Most of his mates would be surprised to know he sometimes puts his thoughts on paper. This was composed after wandering through a decrepit, deserted, hilltop hospital in small-town New Zealand.

Poetry feature:
a eulogy delivered on Hospital road

I've seen pictures of you
When you were younger,
When you were in your prime.
You looked proud.
You looked a mother
Of healthy, bubbling children,
Busy and content.

They say you took the sick and frail,
The young,
The old,
Under your wings.
Nurturing them back to health
As age layered itself upon you
Like coats of hospital-green paint.

Now,
Old and frail yourself,
That picture seems a world
A thousand sheets of flaking paint, away.

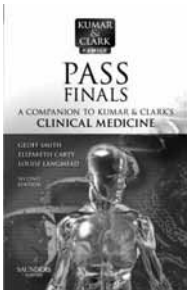
All I see is a grandmother,
Whose children have left her,
At that place atop the hill
On hospital road.

Discarded to die quietly
Amongst the huddled trees,
Bending to weep with you
And mourn your falling.
While you overlook those born out of your heart,
Slowly rotting away piece by piece,
Waiting to be saved.

These titles are available from Elsevier Australia (www.elsevier.com.au) or your favourite university or medical bookshop.

Ahrin Anna Choi
Fifth year Medical Student
Dunedin School of Medicine
University of Otago

Anna is currently a fifth year medical student in Dunedin, with interests in developing world medicine, research and surgery. In the future she hopes to get involved in international health policy.



Pass Finals: A companion to Kumar and Clark's Clinical Medicine, 2nd Edition.
Geoff Smith, Elizabeth Carty, Louise Langmead
Saunders Elsevier
2008
NZRRP: $65

During the clinical years, most medical students grow to love a certain textbook, so much so that it becomes an extension of our bodies during fourth and fifth year, and our saving grace during finals. Whether it's the Crash Course series, the good old Oxford Handbook, or Kumar and Clark, we all have that one textbook that carries us throughout our time in medical school.

For me that book is Kumar and Clark's Clinical Medicine, which is great for the naive fourth year still confused about the difference between interstitial fibrosis and emphysema but not quite so helpful when said student is now in fifth year and in dire need of some quick-fire review. Sure, us die-hard Kumar and Clark fans may have fantasised about spending our summer making study notes for every chapter of this 10cm-thick textbook in preparation for fifth year finals, but alas, fantasies remain fantasies for a reason.

And that's when "Pass Finals: A companion to Kumar and Clark's Clinical Medicine" comes into play.

"Pass Finals" is based on Kumar and Clark and therefore comprehensive, but succinct. This handbook-style text, only 2.5cm thick, is perfect for those with sufficient background knowledge who need to sharpen up on the necessary details to do well in exam situations.

There are sixteen chapters covering core information on basic sciences and disease, with each chapter dedicated to a different area of Clinical Medicine: Clinical Pharmacology, Radiology, Clinical Chemistry, Infectious Diseases, Respiratory Medicine, Cardiology, Gastroenterology and Hepatology, Rheumatology, Dermatology, Endocrinology, Renal Medicine, Haematology, Oncology and Genetic Disease, Neurology, Psychological Medicine, and Statistics and Evidence-Based Medicine.

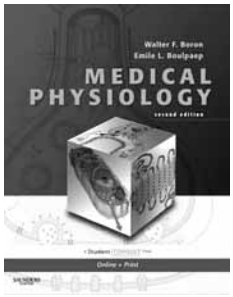
Each chapter includes some background on the system covered, review of necessary examination skills, discussion of relevant investigations, and then onto the diseases in question. All of the text is in bullet-point format, supplemented by clear, simple tables and diagrams, and with references to the corresponding pages of Kumar and Clark (6th Edition) for further reading should any serious gaps in knowledge be discovered. Best of all, at the end of each chapter are a few pages of self-assessment questions (with answers at the back of the text), which will come in handy closer to finals, when MCQs become highly sought-after commodities.

There are also three chapters at the beginning of the book giving helpful tips on sitting medical school examinations in general: "How to pass medical finals," "Question types in medical finals," and "OSCEs." I found the chapter devoted to OSCEs especially helpful. It gave some background on how they are run, general advice on what to do/what not to do, as well as a collection of common OSCE scenarios.

Overall "Pass Finals" is undoubtedly an ideal review book which medical students will find invaluable closer to finals. Regardless of whether you are already a Kumar and Clark fan, or have always been put-off by the sheer thickness of the full textbook, this succinct yet thorough companion will help keep those study-prep freak-outs down to a minimum come October.

Benson Chen
4th year Medical Student
School of Medicine
University of Auckland

Benson Chen is a 4th year medical student at Auckland medical school. He doesn't know what he will end up doing in the future but is currently happy reviewing books.



Medical Physiology, 2nd Edition.
Walter F. Boron, Emile L. Boulpaep
Publisher: Saunders Elsevier
2008
NZRRP $147.00

Many medical students find physiology challenging to learn, mainly because it requires a competent grasp of difficult concepts, which one cannot simply memorise. However, a good foundation in physiology is essential in order to understand clinical medicine. Fortunately, a recent addition to the textbook market has arrived: Boron and Boulpaep's aptly named Medical Physiology.

Big in size, colour and content, the second edition attempts to provide a comprehensive coverage of the medical physiology of the major organ systems from a cellular and molecular basis. The beauty of this book is the editors' attempt to show 'expertise of a multi-author book with the consistency of a single pen'. The editors have recast manuscripts written by Yale professors of physiology into a uniform style. The resulting text is consistent throughout which makes it easy to read and understand.

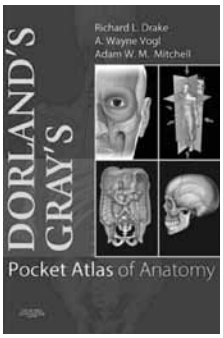
The book is divided into ten sections, structured around the physiology of the major systems. Each section begins with an overview of the organisation of the system being covered. Text in these introductory chapters is presented in a form-function format, which serves as a good review of the basic anatomy and physiology of each of the organ systems. The subsequent chapters then comprehensively cover the physiology in more detail, usually with thorough explanations of the physical principles involved. A reference list is provided at the end of each chapter for those of you who are not satisfied by the sheer amount of physiology presented.

Physiology is usually best understood in a diagrammatic format, and Medical Physiology definitely delivers in this aspect. The text is accompanied by more than 800 high quality full-colour line drawings. I found these diagrams to be incredibly useful, as they clarified the difficult concepts explained in-text. Much of medical physiology deals with pathways, which are often poorly illustrated in physiology texts. Medical Physiology presents these pathways in easy-to-understand flow diagrams and line drawings, which feature balloon captions explaining key processes. The book also comes with internet access to a full online version, with additional features such as a question database reviewing important concepts.

Medical Physiology comprehensively links the molecular and cellular foundations of physiology to organ system physiology, however it fails to integrate any clinical knowledge of disordered physiology at great depth. Although relevant diseases are introduced in boxed sections, these are not covered in enough detail to be considered useful for the clinical years. If you are looking to revise physiology in your clinical years, Medical Physiology is definitely not for you. The sheer amount of detail is overwhelming, not to mention the multitude of equations and derivations which are sometimes distracting. But if you like learning physiology from a biophysics approach, or are looking for an alternative to standard physiology textbooks such as those by Guyton and Hall, or Berne and Levy, Medical Physiology should be on your bookshelf!

Kirollos Kamel
Fourth year Medical Student
Dunedin School of Medicine
University of Otago

Kirollos Kamel is a 4th year medical student at the Dunedin School of Medicine. He has an interest in neurology, internal medicine and neurological research



Dorland's/Gray's Pocket Atlas of Anatomy
Drake RL, Vogl AW and Mitchell AWM.
Publisher: Churchill Livingstone/Elsevier
2008
NZRRP: $65.00

Don't you just dread having to take your huge Gray's anatomy to the anatomy labs? Not only is the large size inconvenient, but the book's weight is just intolerable. What about surgical rounds? Do you sometimes wish you can bring your textbook/Atlas with you, but can't because of the size? If that sounds like you, then your prayers have been answered. "Dorland's/Gray's Pocket Atlas of Anatomy" combines the beautiful and clear illustrations from the latest editions of 'Gray's Anatomy for students' and the original 'Gray's anatomy' and 'Gray's Atlas of Anatomy' with the extensive anatomical definitions from 'Dorland's Illustrated Medical Dictionary' in one convenient handbook about the size of your Oxford handbooks and with similar thickness too, making it the most convenient reference for anatomy when you're out there in the dissection room or on the wards.

The book's layout is best likened to the "Flash-card" Style, where one side of the card has the anatomical illustration with numbers replacing labels, and the other side containing the key to these numbers and a small paragraph on what each structure is. Similarly, Dorland's/Gray's Pocket Atlas is organized in a two-page fashion, where the right page contains one or more anatomical illustrations with numbers replacing labels, and the left page contains the anatomical structure representing each number and a brief but succinct definition. If, for example, you are looking at a muscle, the definition would include its name, origin, insertion, innervation and action. For a nerve, the definition will include the modality (pure sensory, pure motor or mixed), its parent nerve and the area it supplies and the muscles it innervates. For arteries and veins the definition will include origin (or destination for veins), branches and the area supplied/drained by it. So the left page makes for a very juicy summary of what you need to know on the spot, while the right page presents a number of clear illustrations (mostly from Gray's anatomy for students, with a few from Gray's anatomy) compressed to fit into the A3-size pages of the book.

The book is divided into eight chapters, addressing human anatomy by region. Chapter One is a general introduction and is mainly set out to give you the definitions of basic anatomical terms and some of the Latin terms that get repeated often, such as fossa, cavity, retinaculum, eminence etc. The remaining eight chapters are in identical order to Gray's Anatomy for Students, starting with the Back and ending with the Head & Neck. The index is well-organised and even resolves that annoying habit of Gray's of listing all the arteries under the name 'Artery' . If you are looking up a specific artery, you can go directly to the letter its name starts with and find it. Oh, and did I mention that there is a mini-CD that comes with the book which contains Dorland's spell Checker, helping you get the correct spelling whenever you use Word to write anatomical and medical terms?

The book has a few short-comings, which are understandable given that it is a Pocket Atlas. Sometimes they cram too many pictures into one page leading to a crowded page and diagrams that are too small. You may have to squint to see the smaller structures on these diagrams. The book is very deficient when it comes to Brain anatomy, although the arterial supply, meninges and cranial nerves are adequately covered. You should also be aware that the book does have a printing error in pages 402-3 with the labels not quite matching the numbers; however, there are hardly any books around that have no mistakes at all. Finally, the book is quite deficient when it comes to surface anatomy, so don't expect to find all of Gray's clinical anatomy section in there. Having said that, every now and then you may find a real-life picture to illustrate some surface anatomy. Of course, you won't find any of those clinical cases or clinical anatomy notes you see in Gray's Anatomy, but that is normal for an Atlas of anatomy.

In conclusion, I think this book is quite an achievement, because in combining two of the most famous books around, it has an extensive breadth of coverage of regional anatomy whilst retaining its small size. I recommend this book to all medical students and all doctors, no exceptions. And with a price of $65.00 only, you know it's worth it!

NZMSJ author guidelines for submissions

Format requirements

- Use Microsoft Word
- Include figures, legends and tables
- Save as a word document (*.doc)
- Photographs are to be included as separate files

Types of Submission

- Original research articles (<3000 words)
- Feature articles (<3000 words)
- Case reports (<1500 words)
- Book reviews (<500 words)
- Letters (<500 words)

Criteria for Submission

- Submissions are of interest to medical students
- Written approval from research supervisors is required
- Author's email address for correspondence is necessary
- Short blurbs about authors should be included

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- The British Medical Journal house style is to be followed.
- This is available at:
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- Use the Vancouver referencing style, insert numbers within the text using superscript, do not use brackets around the numbers
- Abstracts are required for research articles

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Process

All submissions will be subedited for spelling, grammar and clarity. They will then be sent for expert reviews. Authors will be required to revise their articles during this process.

Final article selection for publication will be made in conjunction with our academic advisors and editorial board once the review and revision process is completed to a professional publishing standard.

Acceptance of an article into the review process does not constitute a guarantee of publication. It is the intention of the NZMSJ to provide authors with the benefit of external review and revision processes that are standard internationally for published journals. This is in keeping with our educational aim to assist medical students in making the transition from writing for medical school to writing as a graduate.

Submissions received before Feb 26, 2010 will be considered for issue 11

In keeping with the NZMSJ's ethos of encouraging students to submit articles, we are proud to offer prizes to acknowledge excellent work. Under the category of academic submissions, **a first prize of $350 and a second prize of $150** will be awarded. The best feature article and letter to the editor will receive **medical book prizes.**

Submissions for the next issue are **due 26th February 2010**.

FACT #2

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