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+ **ALTITUDE ILLNESS**
prevention and management

+ **A SICK BUILDING?**
Wellington medical school

+ **COCHLEAR ATP RELEASE**
developing a cellular biosensor

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Nebulizer mask, metal sanitary box, Kreosote bottle, ear plug cleaner.

Our medical education is constantly being revised. Faculties around the world tirelessly critique and mould their curricula, with each syllabus revision promising greater empathy, empowerment, information literacy and clinical excellence in students. As these changes take place, we challenge faculties to recognize that our education extends beyond our classrooms and clinical teaching. The development of social networking, communication techniques, and student advocacy are a few of the many skills that are refined outside the standard curriculum. Student initiatives provide a valuable forum for the development of these characteristics in medical students.

NZMSJ is representative of the educational and professional benefits of student initiatives. As the executive of NZMSJ we have been privileged to be part of an exceptionally successful student initiative. From humble beginnings a mere three years ago we have become a recognized biannual journal. NZMSJ is becoming a valuable tool for students to gain experience publishing academic articles. This third edition represents our largest issue yet, and we are confident of continued growth in submission numbers. Alongside the growth of the journal, student authors have had the opportunity for detailed expert review of their work, and reviewers have been exposed to student articles as colleagues instead of markers. We believe that all of the students, staff and authors involved in the NZMSJ enjoy many of the learning outcomes curriculum designers strive for.

The diversity of articles in this edition is remarkable. We have published articles from authors as far away as Nepal and the USA, whilst ensuring that New Zealand students have also been well represented. Original research, interesting reviews and topical opinion pieces have ensured that this issue of the NZMSJ will make quite exceptional reading. Letters to the editor in response to any article are welcome.

We are also pleased to announce the winner and runner up for the NZMSJ writing prize advertised in our last edition. The academic editorial board and advisors were immensely impressed by the standard of submissions. We selected Shannon McCarthy's literature review of Folic Acid supplementation for first prize; an excellent example of clear, relevant, interesting writing for students. The Gale *et al.* group from Wellington received runner up for their research into the sick building syndrome at the Wellington School of Medicine. Brian Grainger's original research into ATP release in cochlear cells was commended as an impressive investigation of a complex topic .

We look forward to receiving further excellent submissions.

The NZMSJ Executive

Folic acid supplementation as a preventative for defects of neural tube closure

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Shannon McCarthy is nearing the end of her second year as a medical student at the University of Otago. She recently graduated with a BSc in Anatomy and Structural Biology, and hopes to combine her keen interest in neuroscience with her medical career.

INTRODUCTION

Neural tube defects such as spina bifida and anencephaly are rare birth defects that affect around 0.8 per 1000 total births in New Zealand[1] and are due to failure of the neural tube to close during development. For the past 60 years it has been known that folic acid supplementation is effective in preventing neural tube defects by an unknown mechanism[2]. Since 1993 the New Zealand Ministry of Health has recommended 0.8mg of folic acid per day for first time pregnancies and 5mg per day for high risk (previous NTD pregnancy) women to be taken four weeks prior to conception until the end of the twelfth week of pregnancy[3]. A woman needs to receive daily folic acid before she becomes pregnant otherwise it is too late. This review will examine various intervention studies which have provided strong evidence for the protective role of folic acid supplementation in preventing neural tube defects and the proposed scientific mechanisms of action.

BACKGROUND

Neural tube formation and closure occurs between days 22 and 28 of gestation in humans and involves paired neural folds being brought together at the dorsal midline and adhering to each other with a merging of cells.[4] In mammals, closure is initiated at several places along the anterior-posterior axis until the neural tube forms a closed cylinder which is separated from the surface ectoderm[4]. Neural tube defects (NTDs) occur when various parts of the neural tube fail to close. Spina bifida refers to failed closure of the posterior neural tube. It varies in severity, and is characterised by neural tissue covered by meninges that extrude through the vertebral column[5]. Anencephaly is a lethal malformation that occurs when the anterior neuropore fails to close and the brain remains in contact with the amniotic fluid and degenerates.[5] Epidemiological studies have suggested that environmental and genetic factors have a joint role in causing NTDs[6]. From such studies it has been determined that poor nutrition and folate deficiency in particular puts foetuses most at risk[4]. Folate, or Vitamin B_9, acts as a cofactor for enzymes essential in DNA and RNA synthesis and is also required in the transfer of methyl groups in the amino acid methylation cycle, an essential step in the recycling of homocysteine back to methionine[5].

STUDIES

Several intervention studies have shown that taking folic acid supplements can reduce the occurrence and recurrence of neural tube defects (NTDs). Smithells *et al.* [7] found a significant 85 per cent reduction in the recurrence rate of NTDs in mothers given a multivitamin supplement containing 0.36mg folic acid during the periconceptional period (before conception to early pregnancy), compared with unsupplemented mothers. This trial was controversial however, due to the absence of a placebo controlled double blind approach[8]. In 1988, Mulinare *et al.* [9] found that, as well as multivitamin use reducing the risk of NTDs, it also has a protective effect among women without prior NTD-effected pregnancies.

Milunsky *et al.* [10] found a substantially reduced risk of NTDs among women who took standard doses of folic acid containing multivitamins during the first six weeks of pregnancy, and they estimated that folic acid supplements taken during the first six weeks of pregnancy would prevent the occurrence of NTDs by more than 50 per cent.

The most convincing evidence that folic acid supplementation aids in primary prevention of NTDs and recurrence of NTDs has been provided by three studies. In 1992, a randomised control trial performed by Czeizel and Dudas[11] found that the incidence of a first occurrence of NTDs was reduced among women who took folic acid supplements during the periconceptional period. A placebo controlled study by the MRC Vitamin Research Group (1991) assigned women with previous NTD-affected pregnancies to one of four groups: daily supplementation with 4mg folic acid, 4mg folic acid and other vitamins, other vitamins without folic acid, neither folic acid or vitamins[12]. The trial found that high-dose folic acid supplementation (4.0mg) alone reduced NTD recurrences by 72 per cent and that the addition of other vitamins conferred no extra benefit in averting NTDs[12].

During 1993-1995, the Centre for Disease Control and Prevention in the USA and the People's Republic of China conducted a population based intervention study to the efficacy of periconceptional use of folic acid in preventing NTDs[13]. The study included almost 250,000 women

from northern (high NTD rate) and southern (low NTD rate) China[13]. After finding that periconceptional use of 400 µg folic acid reduced the risk of NTDs by 79 percent for northern China and 41 percent for the southern region they were able to demonstrate that ingestion of 400 µg of folic acid alone per day during the periconceptional period prevents NTDs in areas of both high and low frequency[13].

This strong evidence led the US Public Health Service to recommend 0.4mg per day of folic acid during the periconceptional period as this would reduce the incidence of NTDs by a possible 50 percent[2]. Three approaches to increase folic acid consumption in the US were proposed: improving dietary habits, fortifying foods with folic acid, and recommending the use of dietary supplements containing folic acid[14]. Some population groups were concerned that fortification would expose all members of society to folic acid in larger amounts than was usual[1]. Proposed adverse effects included toxic effects from folic acid ingestion; the masking of vitamin B_{12} deficiency; a relationship between increased folic acid intake and multiple births; and adverse effects with zinc, anticonvulsants, and oral contraceptives[1]. There is no conclusive evidence that folic acid intake produces any of these[1]. After mandatory fortification, a primary mechanism for improving the folate status of the majority of women in the population, of cereal grain products with 140 mcg folic acid per 100g flour the reported prevalence of annual NTD affected pregnancies decreased by 27 percent[14]. The US still recommends that women take folic acid supplements as it is an effective method of ensuring they get the full 400 mcg as diet alone does not provide sufficient amounts[14].

The New Zealand Ministry of Health responded to these various findings by recommending 0.8 mg per day four weeks prior to conception until the end of the twelfth week of pregnancy[3]. For high risk (previous NTD pregnancies) they recommend 5 mg per day[3]. There are many issues regarding supplementation including the fact that most women are still not aware that folic acid prevents NTDs, the use of folic acid remains low, and women who do take supplements are usually not taking them periconceptionally[1]. Many pregnancies are unplanned and NTDs can form before women are even aware they are pregnant.

Current research shows that there are no known toxic effects from folic acid ingestion either by diet, supplementation or fortification. In fact, folic acid has been shown to prevent other birth defects, cancers, and cardiovascular disease[1]. Since 1996 voluntary fortification of certain food products such as breads, breakfast cereals, and food drinks with folic acid has been permitted in New Zealand[3]. Although mandatory fortification would cost initially, the benefits would be far greater. In New Zealand, NTDs are a major component of fetal and infant death and morbidity[1]. They also contribute to the overall 'burden of diease' in terms of medical treatment and other associated costs with spina bifida having the fourth highest lifetime cost from birth defects[1].

PROPOSED MECHANISMS OF ACTION

Although the evidence for scientific mechanisms on how folic acid action prevents NTDs is much less convincing and the underlying causes of NTDs are still unknown, a few explanations have been proposed. A women's risk of having a child with NTD has been found to be associated with early pregnancy red cell folate levels in a continuous dose-response relationship[15]. Their finding that the supply of folate to the embryo may be diminished even with seemingly normal maternal folate levels led Daly *et al.*[15] to believe that susceptibility of NTDs may come from an inborn error of folate metabolism rather than a dietary deficiency[5].

A study in 1996 by Rosenquist *et al.*[16] found that homocysteine, a teratogenic agent at high concentrations, was found in increased levels in folate depletion. Treating avian embryos with folate supplementation prevented this rise in homocysteine to teratogenic levels therefore the primary effect of folic acid supplementation may be to protect against NTDs by reducing the levels of maternal serum homocysteine[16]. Hook and Czeizel[17] found a statistically significant association between folic acid supplementation and an increased prevalence of recognised spontaneous abortion causing embryonic and foetal death. They proposed folic acid as a strong candidate to be a terathanasic agent which may diminish the rate of NTDs by selectively inducing abortion of affected conceptuses.

Five to fifteen per cent of the general population is homozygous for a thermolabile variant of 5,10 methlenetetrahydrofolate reductase (MTHFR), a folate-related enzyme which is positively associated with the risk of NTDs[18]. Molloy *et al.*[18] found that plasma and red cell folate levels were significantly reduced in women homozygous for this variant causing an additional requirement for folate. This may be the first genetic risk factor for NTDs to be identified and is estimated to account for 13 percent of all cases[5].

Antony & Hansen[19] hypothesised that folate receptors were critical for neural tube development because when they were eliminated in mice a high percentage of folate-responsive NTDs were reported. They proposed that a reduction in folate receptor expression would reduce fetal folate delivery causing decreased proliferation of neural tube cells in early pregnancy leading to NTDs. Saitsu *et al.*[20] agreed with these findings that folate receptors have an important role in embryogenesis. One such receptor is folate-binding protein 1(FBP1), a membrane protein that binds folate with a high affinity and incorporates it into cells by endocytosis[20]. Saitsu *et al.* completed a study on FBP1 and discovered it is mainly localised to the most dorsal regions of the neural folds and is expressed prior to dorsal closure of the anterior tube. They also found that folate transport through the human placenta and mouse yolk sac was mediated by FBP1 at the stage of neural tube closure. Therefore a defect in FBP1 expression could explain how a deficiency in folate leads to NTDs.

Genetic variants of folate-pathway enzymes or folate receptors do not account for the 70 per cent reduction in NTDs associated with folic acid supplementation. However, Rothenburg *et al.*[21] identified autoantibodies against the folate receptor membrane protein in serum from women who had a previous pregnancy complicated by an NTD. Folate responsive NTDs may be due to the autoantibody binding to folate receptors on placental membranes and cells with a high affinity and inhibiting the binding and uptake of folate[21]. Folic acid may bypass this autoantibody-mediated blocking of cellular folate uptake as it is reduced and methylated in vivo and transported into cells by another membrane protein, reduced-folate carrier (RFC)[21]. Folic acid also has a high affinity for the folate receptor so may displace an autoantibody with a lower affinity and explain why folic acid supplements are more readily absorbed than folate naturally contained in food[21]. This would provide a mechanism for how folic acid supplementation can dramatically decrease the recurrence of NTDs.

In New Zealand, NTDs are a major component of fetal and infant death and morbidity.

CONCLUSION

There is strong evidence from epidemiological studies that folic acid supplementation can prevent defects of neural tube closure. This has led the NZ Ministry of Health to recommend a 0.8 mg daily intake for all women before conception and during early pregnancy, and higher doses to prevent the recurrence of NTDs in women with a previously NTD-effected pregnancy. Although it is still unclear as to how folic acid acts to prevent NTDs such as spina bifida and anencephaly, several explanations have been proposed which implicate various other factors in depriving the highly proliferative neural tube cells of folate during the period when they need it most, neural tube closure.

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Is the Wellington medical school facility a sick building?

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ABSTRACT

The sick building syndrome (SBS) is an occupational health description that indicates a high prevalence of certain symptoms in a building's occupants. This article describes a pilot study that was undertaken to determine whether Wellington School of Medicine and Health Sciences (WSMHS) facilities suffered SBS. An internationally validated questionnaire was delivered to staff electronically. The response rate was 60%. The prevalence of work related symptoms was found to be similar to international studies (mean 1.76 symptoms per person, from list of five), with a similar detrimental effect on productivity. As in previous research, gender and job were found to be major contributing factors to SBS symptoms, but no locations within WSMHS were found to be better or worse than others. Environmental causes of SBS may vary widely between nearby work areas. Detailed, systematic study is required to elucidate environmental causes of SBS in New Zealand.

Keywords

Sick Building Syndrome, indoor air quality, gender, occupation

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INTRODUCTION

The term sick building syndrome (SBS) is applied to a building in which certain non-specific symptoms are more common amongst the occupants than in comparable buildings[1]. The symptoms are present when the person is in the affected building, and alleviated when the person is away from the building. It is a heterogeneous clinical picture, comprising headache, lethargy, with dryness or irritation of the eyes, nose, throat or skin[2]. The symptoms are common amongst office personnel (over 80% experience one or more), but generally occur with low severity, and in different combinations[3]. The SBS is defined by prevalence: sick building occupants suffer from an average of more than 2.5 work-related symptoms each (occurring at least twice in 12 months, improving away from the building, from a list of five symptoms) while the healthiest buildings have fewer than 1.5 building-related symptoms per occupant per year[3]. Thus, the diagnosis of SBS requires systematic research across all building occupants.

Sick building syndrome is due to the interaction between many personal factors (e.g. gender, medical history), occupational factors (e.g. clerical work, proximity to photocopiers, computers), psychosocial factors (e.g. stress, job satisfaction), and environmental factors (e.g. indoor air quality, lighting, temperature, crowding). All of these (and more besides) are associated with, and seem to contribute to, SBS symptoms[3-9]. Some of these factors may be the primary causes of SBS, but others will be simply confounding relationships, indicators of susceptibility, or markers of exposure.

There have been SBS-like complaints about the work environment at the Wellington School of Medicine and Health Sciences (WSMHS) for many years, the buildings are typical of those that suffer SBS, and it has been studied in the past[10]. This study aimed to determine whether WSMHS suffered SBS using internationally standardised methods, and to describe the work locations and other factors that were associated with these complaints.

METHODS

The target population were staff and postgraduate students working at least ten hours per week in the two main buildings of WSMHS. Workers who spent less time in WSMHS would introduce confounding effects from other workplaces. The Academic and Link buildings stand adjacent, contain a wide variety of work environments, and are supplied by three sealed mechanical ventilation systems: designated A, B (Academic) and C (Link). Only A and B systems contained humidifiers, and system A recycles 30% of the air returning from office spaces, but otherwise the systems had equivalent construction.

The study was approved by the Wellington Regional Ethics Committee, and was supported by the Dean, Professor Nacey.

A questionnaire was developed from that of the SBS advisory group to The Royal Society of Health (RSH) of the United Kingdom. The RSH questionnaire was designed by an international committee to standardise the screening of buildings for SBS, and was validated both in terms of reliable prevalence estimates and the detection of clinically accurate symptoms[3 11 12]. The questionnaire was piloted on six staff outside of the buildings, and minor comments were incorporated.

The questionnaire contained questions on symptoms, and potentially associated variables (i.e. personal, psychosocial, occupational factors and location). The eight SBS symptoms investigated were 1) dry eyes, 2) itchy or watery eyes, 3) blocked nose, 4) runny nose, 5) dry throat, 6) headache, 7) lethargy and 8) dry, itchy or irritated skin. Symptoms were only included if they were confirmed as "better on days away from WSMHS." Each symptom had to have occurred on at least two separate occasions in the preceding 12 months.

The questionnaire was delivered as a Microsoft Word attachment to all WSMHS e-mail addresses (a method use with previous success[13]). E-mail is a fast and cost-efficient survey method, but can introduce new difficulties (e.g. subject identification and redundant addresses)[14 15]. It was estimated that over 90% of the target population were included in this e-mail list.

The questionnaire was delivered to 252 valid e-mail addresses, and non-responders received a reminder at seven days and hard copies at three weeks. Fifty-nine recipients did not spend more than ten hours per week in the two buildings (and were excluded), creating an accessible population of 193 addresses.

Results of the RSH questionnaire are calculated by the mean number of symptoms per respondent (from the list of eight). This is termed the person symptom index, PSI_8, and when averaged across a building, is the building symptom index, BSI_8. The PSI_5 and BSI_5 (from a list of five symptoms), exclude skin symptoms, runny nose and irritated eyes, have a more predictable distribution and can be compared to the BSI_5 of 42 British buildings[3]. The PSI_8 and BSI_8 are more sensitive to small differences, so were used for factor analyses in this study. Occupation was grouped into six categories, involving similar tasks, status and income. Statistical analyses used chi-squared (X^2), the Kruskal-Wallis Test (a non-parametric ANOVA, which produces the statistic H, with a X^2 distribution), Wilcoxon Two-Sample Tests (a non-parametric t-test), and multiple logistic regression models on SAS 8.0 (Cary, NC, USA) and SPSS v10.1 (Chicago, IL, USA) software packages.

Table 1. The Building Symptom Indices of Wellington School of Medicine and Health Sciences

Building (n)	Ventilation system – area (n)	BSI_8	BSI_5
Total (106)		2.45	**1.76**
Academic (69)		2.29	**2.05**
	A (39)	2.03	**1.49**
	B - Library (10)	1.50	**1.00**
	B - Animal facility (2)	5.00	**3.50**
	B - All other areas (18)	3.22	**2.17**
Link (37)	C (37)	2.74	**1.71**

RESULTS

From the 193 target e-mail addresses, a total of 114 completed questionnaires were returned (overall 60% response). Only 31% of the respondents were men, and they were significantly older than the women, with higher levels of formal education and more senior academic positions than female respondents. None of the other medical, occupational, psychosocial or environmental factors differed significantly between the genders. There was no information available on non-responders, so it was not possible to assess responder bias objectively.

Overall, respondents reported an average of 2.45 work-related SBS symptoms (from the list of eight, while the BSI_5 was 1.76). Only 27% of respondents did not report any of the eight work-related SBS symptoms, and 57% experienced at least two symptoms (which is described as an important level for effects on productivity[16]).

The BSI for areas of WSMHS are shown in Table 1. The BSI_8 (or BSI_5) did not differ significantly between these five ventilation areas, despite the wide range of symptom rates (Kruskal-Wallis, $H_{(4)} = 8.97$, $p = 0.062$). Logistic regression could not adjust for gender and job position, because respondents from some locations were entirely female, or of one job type. Alternative models, using broader location zones, found no differences in prevalence after adjustment for gender and occupation. The floor, or room type of the occupant were not associated with symptom prevalence either.

Women suffered more symptoms (PSI_8 2.91, PSI_5 2.09) than men (PSI_8 1.35, PSI_5 1.00), as tested by the Wilcoxon Two-Sample Test (PSI_8: $S_{(75, 34)} = 1325$, $p < 0.001$). Unadjusted odds ratios (uOR) indicated that women suffered significantly more lethargy (3.35, 95% CI 1.4–8.1), blocked nose (3.29, 95% CI 1.2–8.9), dry eyes (8.57, 95% CI 2.4–30.5) and irritated eyes (4.47, 95% CI 1.4–14.0).

Job position was also associated with PSI_8 ($H_{(5)} = 24.9$, $p < 0.0001$). Senior academic staff (of whom 68% were men), suffered fewer symptoms (PSI_8 1.09) than library staff (PSI_8 1.63), followed by clerical/secretarial (PSI_8 2.89), research (PSI_8 3.12), managerial (PSI_8 3.33), and technical staff, who suffered most (PSI_8 4.08).

Several other factors were associated with PSI_8 on univariate analysis. An attempt was made to correct for the large number of interacting factors, using sequential logistic regression. The result modelled the odds of suffering each symptom, adjusted for gender, job position, subjective ratings of indoor air quality, air movement, lighting and overall comfort, computer use, photocopying, and history of asthma, rhinitis or conjunctivitis. The adjusted odds ratios (aOR) for gender were not significantly different to 1.0, with the exception of dry eyes, which women were 7.69 times more likely to suffer, after adjusting for other factors, (95% CI 1.80–32.8). Some other symptoms appeared associated with gender (e.g. lethargy aOR 4.15, 95% CI 0.93–18.6; dry throat aOR 0.46, 95% CI 0.11–1.87), but the model did not have sufficient power to detect this.

DISCUSSION

Overall, workers in WSMHS facilities suffered an average of 2.45 work-related SBS symptoms each and 73% of respondents reported at least one. This means the WSMHS facilities were not particularly 'sick buildings' by international standards, and compared favourably to British building with similar ventilation systems[2]. The reported symptom rates were generally lower than were found in Palmerston North buildings, or the UK study (except for women suffering dry eyes)[17]. It would seem then, that WSMHS has SBS symptoms at similar, if not healthier, rates to comparable buildings.

A total of 57% of respondents reported at least two work-related symptoms, a similar

proportion to a Palmerston North study, and the large British study[3 17]. This is reported as the level at which symptoms negatively affect productivity[16], and this result is therefore relevant to building managers at WSMHS.

A possible source of selection bias in this study was the e-mail delivery method, which excluded workers without e-mail. These workers would have different work characteristics (and thus may suffer more or fewer SBS symptoms), but it was not possible to assess these differences accurately. The e-mail method also targeted redundant addresses, and introduced avoidable problems of subject identification and localisation. All of these problems could be corrected in future studies by defining the accessible population with human resources data, and then identifying their e-mail addresses if available. The modest response rate of 53% makes selection bias a greater possibility, and is another limitation of this study. However, the methods used in this study have been shown to have validity and reliability in previous international research [11 12 13].

Within WSMHS, no areas were found to have significantly worse SBS prevalence than others, despite a wide range of values (BSI_s between 1.0 and 3.5). This suggests that any causative environmental factors were either variable within the large location zones, or were weak compared to the overlying heterogeneity of SBS and personal/occupational factors. The associations between individuals' environmental perceptions and SBS symptom rates might suggest the former.

Gender and occupation (and occupational factors) were interrelated, and were both strongly associated with SBS symptoms. Both of these associations persisted after adjustment for many covariates. It is not known why women suffer more symptoms than men[5 9], but job-related factors are much easier to hypothesise (e.g. level of control over work and environment). However, in this study none of the many occupational or psychosocial factors that were investigated were predictive of symptoms in the multiple regression model.

In summary, SBS symptom rates in WSMHS facilities were found to be comparable to office buildings studied in Britain and New Zealand. Consistent associations between gender, occupation and SBS symptoms explained more of the variation than did workers' location within WSMHS. In buildings where SBS is suspected, detailed investigation is required to provide evidence from which building management decisions can be made.

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A different type of preventive medicine

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With the growing number of terrorist attacks disrupting the everyday lives of common people and with the fear of such attacks growing in society, our world is not only faced with the problem of responding to such events, but with the bigger challenge of preventing them from happening. In 1981, the World Health Assembly declared that "the role of health workers in the preservation and promotion of peace is the most significant factor for the attainment of health for all". However, this statement has yet to go beyond words into actions. Although healthcare professionals are among the first to react in crises and are also one of the more essential parts of a crisis relief team, there is a lack of involvement from their part in preventing such crises. Medical professionals should not limit their mission to treating the effects of war and conflict, but should also cooperate with Government and Military bodies to help promote and sustain security.

Conflict disrupts infrastructure and essential services such as medical care and sanitation. It affects trade and the economy of the whole population. It impairs food and water production and distribution, and also displaces communities from their homes. All these have a health component or a health impact. As with other medical issues, doctors should deal with etiology and prevention, and not only treatment. Therefore, in view of the needs of the current world, an exclusively biomedical model of death and disease that deals only with the effects of war and has no conflict prevention component is no longer sufficient in today's context.

Public health is still insufficiently used as a tool against terrorism and conflict.

Medicine is a bridge between societies because it sets out common concerns for prevention and care and through this it may hold the potential to protect World peace. Public health is still insufficiently used as a tool against terrorism and conflict. It has been stated that public health, by tackling issues such as harm reduction, disease and poverty and using population approaches to health and social medicine, "might do more good than air marshals, asylum restrictions and identity cards"[1]. However, the various bodies that act towards securing world peace still do little to involve health professionals in the planning of their activities and agendas. Neither do they promote an interest in peace-keeping actions among these professionals. There are medical professionals that are active and enthusiastic fighters for peace, but looking at the general picture, there are still not enough of these individuals involved in high-level decision making within the respective bodies that are responsible for maintaining security and peace.

Irina has spent this year abroad as a Rotary Ambassadorial Scholar in Albert-Ludwig University Freiburg, Germany. Besides the clinical aspects of medicine, she is also interested in "alternative" areas like public health and medical journalism. She is a student adviser for Student BMJ, and has carried out internships at British Medical Journal, World Health Organisation and Harvard School of Public Health. She highly enjoys working in international environments and travelling is one of her greatest pleasures.

The problem is not only at one end. There is also a lack of awareness, skills and leadership among health professionals concerning their possible roles in targeting root causes and preventing the incidence of war. Although there has been some recent movement in Medical schools towards introducing "Peace through health" as an academic discipline, still very few do so. As such, most medical students worldwide leave universities unprepared and unaware[2]. However, by the nature of the medical profession, most health professionals have or develop a humanistic spirit and dedication for humanity. Their input might be invaluable in finding solutions for preventing conflicts.

If medical professionals go beyond the curative perspective towards a more visionary one, they can act as a link between Security and Health, thereby filling in some gaps by helping secure world peace though one of its core elements: Health.

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A new way to look at the obesity epidemic: a perspective from my summer studentship

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Obesity is becoming one of the major health issues of our lifetime. Over the last 25 years the prevalence of obesity has doubled in New Zealand adults.[1] However, even more alarming is that this once adult disease is increasing in our children. The Children's Nutrition Survey found that 31 per cent of New Zealand children were overweight or obese, with this figure being over half in some population groups.[2] Egger and Swinburn,[3] state that we need to move away from the traditional view of obesity and take an ecological approach, regarding obesity as a normal response to an abnormal environment:

'To combat the obesity epidemic we first need to cure the environment.'[4]

This environment has been termed the 'obesogenic' environment, and results in an environment which promotes both overeating and physical inactivity.[4]

There are many factors in this 'obesogenic' environment, but one that is very topical currently is the advertising of high-sugar and high-fat foods to children. The situation is summarised well by Saatchi and Saatchi, a leading international marketing company:

'Children are much easier to reach with advertising. They pick up on it fast and quite often we can exploit that relationship and get them pestering their parents.'[5]

Before starting medicine, Anthony completed a BSc degree in human nutrition. As a result he has a large interest in obesity research, especially childhood obesity. He has another summer studentship this year examining food advertising around sports venues in Wellington.

Children are an ideal market because they not only spend billions of their own money, but even more of their caregiver's money (through persuasion and 'pester power'). In the United States it is estimated that children under 12 spend $25 billion of their own money but may influence another $200 billion of spending.[6] The Hastings report is one of the largest reviews of the effects of food promotion on children.[7] The report describes the 'big 5' product companies as the central players in advertising; comprising sugared breakfast cereals, confectionary, savoury snacks, soft drinks and fast food companies. The most important finding, however, was that advertising influences both food preference and purchase behaviour. Essentially this means that advertising affects what children like but more importantly what they spend their money on.

Television advertising is the main medium used by food companies, with upwards of 75 per cent of advertising being spent in this area.[7] In New Zealand, research has found that food advertising during children's television viewing hours is relatively unhealthy and predominantly features foods high in sugar, fat and/or salt.[8] However, there have been no published studies of outdoor food advertising in New Zealand or elsewhere. Furthermore there has been no work on the 'obesogenic' environment around schools – despite some work by Carter and Swinburn [9] assessing the 'obesogenic' environment inside primary schools. My studentship therefore attempted to examine the food advertising and food availability environment around secondary schools in this country, and was published in the 15 July edition of the New Zealand Medical Journal.[10]

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Altitude illness

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Laxmi Vilas Ghimire is a fifth year medical student in Kathmandu, Nepal. He is an active member of the Mountain Medicine Society of Nepal (MMSN), and has attended many a workshop on mountain illnesses. He has previously published articles in the Student British Medical Journal, British Medical Journal, and the Journal of Young Investigators. Laxmi, and the co-author Matiram Pun, have just been appointed the editors of the student section of the Nepal Journal of Neuroscience. Matiram is a fourth year medical student, and an executive of the MMSN. He attended the MMSN and Himalayan Rescue association's Gosaikund Health Camp at altitude of 4380m of Nepal Himalayas, and has presented several papers at national workshops.

Mountains cover one fifth of the earth's surface and are popular destinations for recreation, such as trekking, mountaineering, skiing, deployment of armies and pilgrimages. More than one hundred million people live permanently at altitudes higher than 2500m[1]. With increased numbers of visitors to high altitudes, the prevention and management of altitude-induced illness has become of increased importance to expedition doctors, general practitioners and travel medicine specialists. It has become a public health concern. In this brief review, we will define high altitude illness, it's associated terms, and highlight key scientific principles related to acute mountain sickness (AMS),

The pilgrims seeking health care in the health camp organized by Mountain Medicine Society of Nepal (MMSN) and Himalayan Rescue Association Nepal (HRAN) at sacred Lake Goshain Kund at 4380m in Nepal Himalayas during the festival.

With increased numbers of visitors to high altitudes, the prevention and management of altitude-induced illness has become of increased importance.

The mountains of Nepal Himalaya. **Matiram Pun** (centre) with friend and Buddhist Monk.

high altitude cerebral edema (HACE), and high altitude pulmonary edema (HAPE). Finally we will provide practical recommendations to those ascending to altitude.

Altitude illness is anticipated in those travelling to higher than 2500m though most forms are mild. However a few might encounter life threatening conditions and even death if they are not treated on time. High altitude illness is a collective term for AMS, HACE and HAPE. It is used to describe the cerebral and the pulmonary syndrome that develops in unacclimatised people after ascent to high altitude.

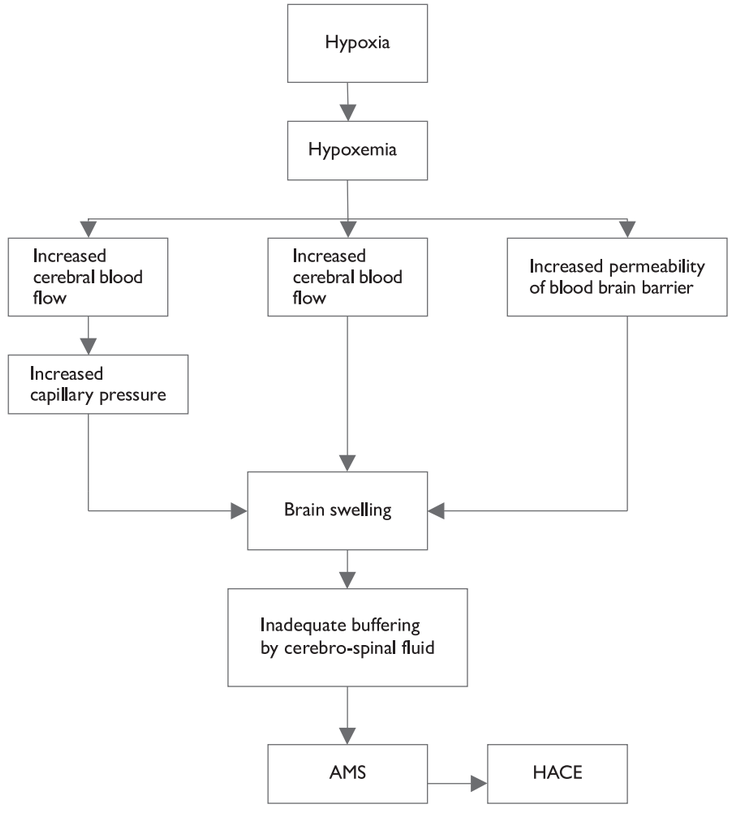

Figure1: pathophysiology of acute mountain sickness and high altitude cerebral edema[1]
(Reproduced with permission from Buddha Basnyat, the corresponding author of the cited article)

The most important risk factors for the development of high altitude illness are the rate of ascent, altitude reached (especially the sleeping altitude), and individual susceptibility. There is no associated susceptibility to age and sex. Physical fitness is not a protective factor against high altitude illness. Vascular endothelial growth factor (VEGF) production in hypoxia has supported the hypothesis that angiogenesis may be involved in HACE,[2] and the sustained plasma VEGF at high altitude is a feature of subjects more prone to AMS[3].

Although there is no hard and fast rule to define different levels of altitude, generally the altitude from 1500-2500m is called intermediate altitude; 2500-3500m as high altitude; 3500-5800m as very high altitude and the height above 5800m is known as extreme altitude.[4]

As one goes higher up a mountain the partial pressure of oxygen is decreased so the body must adjust to having less oxygen. A number of physiological changes that occur to enable the body to function optimally in the low oxygen environment is known as acclimatisation, lack of which is the cornerstone to altitude illness and it can be achieved only through slow ascent.

ACUTE MOUNTAIN SICKNESS (AMS)

Acute mountain sickness consists of a constellation of non-specific symptoms. Specific symptoms include anorexia, nausea, vomiting, insomnia, dizziness, lassitude or fatigue and light-headedness. Headache is the cardinal symptom. Presence of headache in an otherwise healthy individual at more than 2500m altitude is thought to be AMS. These symptoms appear 6-12 hours after the arrival to a new altitude and resolve after 1-3 days in the same altitude. The diagnostic physical signs are lacking so there is a need to differentiate mountain sickness from conditions like exhaustion, dehydration, hypothermia, alcohol hangover and migraine.

Although the exact pathophysiological process of AMS is unclear, symptoms are thought to be due to cerebral swelling either from vasodilation induced by hypoxia or through cerebral edema.

The main principle of the treatment of AMS is to prevent further ascent until the symptoms resolve. Rest at the same altitude usually resolves the symptoms; the patient should improve without treatment within 24-48 hours. If the symptoms deteriorate one should descend as soon as possible. Descent of only 500-1000m leads to the resolution of symptoms of acute mountain sickness.

Medical therapy plays an important role when descent is not possible or supplemental oxygen is unavailable. Acetazolamide, a carbonic anhydrase inhibitor, works by increasing the bicarbonate excretion in the urine, making the blood more acidic, which consequently drives ventilation, which is the mainstay of acclimatisation. Doses of 250mg eight hourly have been used widely and found to be effective to reduce the AMS symptoms. Dexamethasone (8mg initially and then 4mg every six hours) have also been effective in relieving AMS symptoms. Simple analgesics and antiemetics would reduce headache and nausea in early forms of AMS.

Allowing time for acclimatisation through gradual ascent is the best strategy. Once above 2500m sleeping altitude should not be increased by more than 300-600m in 24 hours and an extra day should be added for acclimatisation for every increase of 1000-1200m. 'Climb high, sleep low' should be the guiding principle. Although rate of acclimatisation for individuals vary, a large part of acclimatisation occurs over the first one to three days. Acetazolamide 250 mg twice daily taken one day before ascent has been effective to prevent the symptoms of AMS[5] although, 125 mg twice daily has recently been found effective[7].

HIGH ALTITUDE CEREBRAL EDEMA (HACE)

High altitude cerebral edema has been widely viewed as the end stage of AMS and is generally preceded by the symptoms of AMS. It is a clinical diagnosis, defined as the onset of ataxia, altered consciousness in someone with AMS. Other symptoms are weakness, disorientation, loss of memory, hallucination and psychotic behaviour. It might progress to coma and death due to brain herniation. HACE is commonly associated with retinal haemorrhage, palliloedema and cranial nerve palsy and occasionally focal neurological deficit. In persons with HAPE, severe hypoxemia may lead rapidly from AMS to HACE.

In both brain and lung, at high altitude, hypoxia elicits neurohumoral and haemodynamic responses that result in overperfusion of microvascular beds, elevated hydrostatic capillary pressure, capillary leakage and consequent edema[5]. Fluid accumulation in the brain is thought to be caused by cytotoxic edema, vasogenic edema or both.

HACE is considered to be the end stage of AMS. Anyone with symptoms of AMS should follow three principles: stop further ascent until symptoms have resolved, descend if there is no response to medical treatment, and quickly descend at the very first sign of HACE. Otherwise it might prove fatal.

Dexamethasone (8mg initially then 4mg six-hourly orally) [5] will relieve some symptoms that would make evacuation easy. Oxygen, if available, should be used to aid evacuation. Hyperbaric chambers improve oxygenation and relieve symptoms thus simulating descent to a lower altitude.

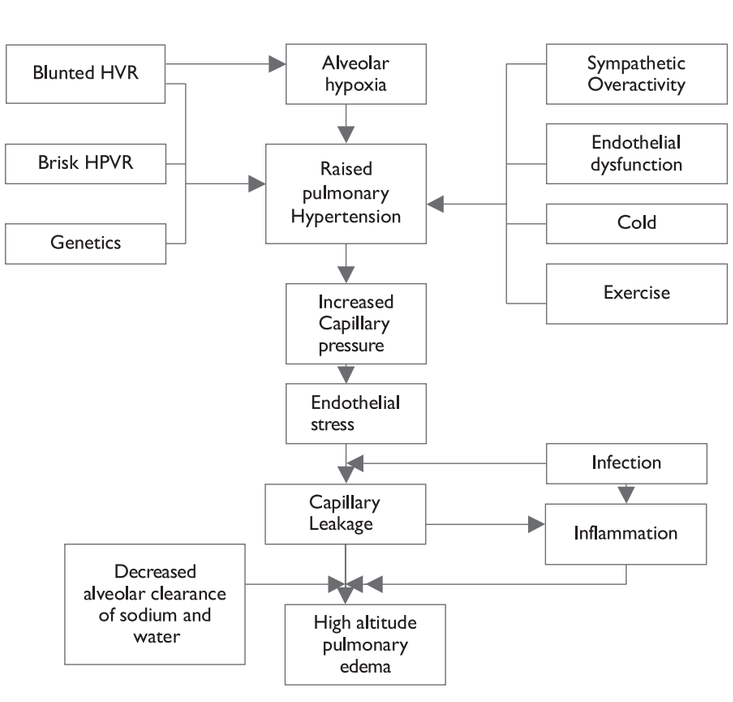

Figure 2: Pathophysiology of high altitude pulmonary edema[1]

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HVR = hypoxic ventilatory response
HPVR = hypoxic pulmonary vascular response

HIGH ALTITUDE PULMONARY EDEMA (HAPE)

High altitude pulmonary edema is at the severe end of spectrum of symptoms of AMS which occurs in persons who ascend rapidly to a height of more than 2500m. It might also occur irrespective of the symptoms of AMS. Vigorous men are more susceptible to it. Other risk factors are strenuous exercise, cold weather and recent respiratory tract infection. Those who have had HAPE in the past are likely to get it again.

Early symptoms are dyspnoea on exertion and decreased exercise tolerance greater than expected for that altitude. Cough, tachypnoea, tachycardia, orthopnoea, cyanosis, rales and frothy pink sputum are the important clinical signs. Fever (38.5^0) is a common feature. HAPE is commonly accompanied by the signs of HACE. Symptoms occur 2-4 days after rapid ascent, and usually begin at night time rest.

HAPE is a non-cardiogenic pulmonary edema associated with pulmonary hypertension and elevated capillary pressure. Furthermore, individuals susceptible to HAPE have exaggerated rise in pulmonary artery pressure in response to hypoxia and exercise. The mechanism for this response includes sympathetic overactivity, endothelial dysfunction and greater hypoxemia resulting from poor ventilatory response to hypoxia.

Early recognition is the first key step in the treatment of HAPE, after which descent and supplementary oxygen are very effective treatments. 10mg nifedipine followed by 20mg slow release preparation every 12 hours may be useful as an adjunct to descent and oxygen[4].

Those with a previous history of HAPE should consider slower ascent to high altitude, try to recognize symptoms early and consider nifedipine prophylaxis 20mg slow release preparation every eight hours[7]. Inhaled ß-agonist has also been effective in preventing HAPE.

CONCLUSION

People face both danger and pleasure in the high mountains. Lack of acclimatisation is the main culprit in presentations of AMS, HACE and HAPE. To become acclimatised, slow ascent should be our motto for the prevention of high altitude illnesses. The message is loud and clear: "Climb every mountain but slowly!" Over exhaustion, alcohol and dehydration inhibit acclimatisation, and must be avoided at high altitudes. If necessary, take Acetazolamide prophylactically. If you get altitude illness, firstly stop your ascent, secondly take medical treatment, and thirdly descend. Drugs are used mainly for symptomatic relief and not so much for treatment - prevention is paramount.

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Imaging ATP Release in the Cochlea: The Development of a Novel Cellular Biosensor

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ABSTRACT

The aim of this study was to develop a novel biosensor that can be used to detect ATP release from cochlear tissues. Chinese hamster ovary (CHO) cells were transformed by cotransfection with linearised pcDNA3.1 plasmids containing an enhanced Green fluorescent protein (eGFP) reporter gene (pcDNA3.1–eGFP) and the endogenous $P2X_2$ subunit which assembles to form ATP-gated ion channels (pcDNA3.1–$P2X_{2-1}$). Expression of the eGFP was detected using confocal microscopy and expression of the P2X receptors was detected using a whole cell patch clamp.

Transfected cells showed a 11 per cent response rate (n = 46) following exposure to 100μM ATP under whole cell patch clamp, which produced inward ATP-gated currents that ranged from –31 to –1350 pA (mean current response = –934.03 ± 416.38pA) with a mean reversal potential ($V_{z\ ATP}$) of –21 ± 7mV. This corresponded closely with the proportion of cells which showed GFP fluorescence.

Confocal imaging of intracellular calcium levels ($[Ca^{2+}]$) was also considered as a means of detecting ATP activation of the $P2X_2$ receptors. CHO cells were loaded with a $[Ca^{2+}]_i$ indicator dye (Fluo-4AM) and then exposed to 40μM ATP. In both untransfected and $P2X_{2-1}$ transfected CHO cells, this revealed a large, rapid increase in $[Ca^{2+}]_i$ (mean peak F/F_0 = 6.0 and 4.2 respectively, where F = fluorescence at peak and F_0 = control fluorescence prior to ATP application). This is attributable to P2Y receptor coupling of intracellular calcium release from the endoplasmic reticulum as previously reported.

In summary, this study has shown that CHO cells can be used as a biosensor to detect extracellular ATP, either by transfection of P2X receptors for sensitive detection of ATP-gated membrane currents, or by imaging of calcium release using confocal microscopy.

KEYWORDS

Cochlea, CHO cells, P2X receptor, ATP, Noise-induced hearing loss

ACKNOWLEDGEMENTS

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Brian Grainger is currently in the third year of a Bachelor of Science degree in Biomedical Science and hoping to enter medicine as a graduate in 2006. This research was conducted in the Molecular Physiology laboratory, part of the Auckland Auditory Neuroscience Group, as a summer studentship over the summer of 2004/2005.

INTRODUCTION

Noise Induced Hearing Loss (NIHL) is a significant cause of disability and is estimated to affect approximately 120 million people worldwide[1] including 390,600 New Zealanders[2]. The effects of NIHL are known to compound with age, resulting in sensory deprivation, loss of communication skills, social isolation and loss of self-esteem[3,4,5] all of which have a compounding detrimental effect on the patient's overall quality of life.

Protection of the cochlea from damage caused by exposure to excessive noise levels is believed to involve a two tiered system. The first level of protection is provided by the olivocochlear bundle (OCB), the efferent neural fibres of the cochlea which reduce the signal transduction activity of the hair cells through cholinergic-synapse-induced hyperpolarisation[6,7]. However, this mechanism becomes less effective at sound levels beyond about 80dB and consequently, sound levels approaching 90dB result in temporary threshold shift (TTS) and those in excess of 110dB result in permanent threshold shift (PTS)[8].

The second level of protection involves ATP release and signalling to specific ATP-gated ion channels, assembled from two broad molecular classes of receptor subunit; P2X and P2Y[9]. ATP levels in the cochlea are known to increase in response to noise exposure[10] following release from vesicular stores in the stria vascularis[11], and the supporting cells (Hensen's cells) of the organ of Corti[12]. ATP molecules subsequently bind to and activate the P2X and P2Y receptors leading to a reduction in the endocochlear ionic potential which provides the driving force for signal transduction at the sensory hair cells[9] and thus a consequential preservation of hearing function.

This study aims to develop a cellular biosensor to detect the release of ATP within the cochlea by using genetic engineering technology to express the gene for the $P2X_2$ receptor in a cultured mammalian cell line and then positioning these cells at various sites within the cochlea and using the magnitude of $P2X_2$ receptor response to ATP as a measure of endogenous ATP release within the cochlea. The potential of knowledge of this homeostatic process to provide opportunities for the clinical treatment of NIHL has been enhanced by the discovery that administration of ATP to hearing impaired guinea pigs resulted in detectable improvements in cochlea function[13].

METHODS

CHO Cell Transfection

Chinese hamster ovary (CHO) cells (Gibco) were maintained in 200mL Dulbecco's modified eagle medium (D-MEM) (Invitrogen) supplemented with 1 per cent non-essential amino acids (NEAA) (Invitrogen), 1 per cent streptomycin and penicillin (S/P) (Invitrogen) and 10 per cent fetal bovine serum (FBS) (Invitrogen). Prior to transfection, 2×10^5 cells were seeded into 24-well plates and made up to a total volume of 1mL using modified Eagle's minimal essential medium (Opti-MEM) (Invitrogen) and then incubated at 37°C in 5 per cent CO_2 for 24 hours.

Cell transfection was carried out with cotransfection of pcDNA3.1–$P2X_{2-1}$ (Invitrogen; kindly supplied by Mrs. Denise Greenwood) and pcDNA3.1–eGFP (Invitrogen; kindly supplied by Mrs. Carol Wang), with the identity of the $P2X_{2-1}$ insert validated by restriction endonuclease digest (see Fig. 1A). This combined mixture was then aliquoted into the wells of a 24-well cell plate seeded with 2×10^5 CHO cells (see Fig. 1B) in 500μL Opti-MEM media to obtain a final concentration of 800ng DNA in each well. The cells were subsequently incubated at 37°C in 5 per cent CO_2 for 24 hours. Transformation of CHO cells with the gene constructs was confirmed by fluorescence microscopy, based on detection of expression of the eGFP reporter.

Electrophysiology

Whole cell patch clamp recordings of successfully transformed CHO cells were made as previously described for cochlear hair cells[14] 24, 48 and 72 hours after transfection. Cells were placed in a 200μL recording bath mounted on an inverted microscope (Nikon, Japan). The bath contained a standard external solution (composition in mM: NaCl 150, KCl 4, Na_2HPO_4 8, NaH_2PO_4 2, $CaCl_2$ 1.5, $MgCl_2$ 1.0, D-glucose 1.0, pH 7.25 with 1M NaOH, osmolarity = 320mOsmol). Bath solutions were exchanged through rapid bath superfusion (300-500μL/min^{-1}) via a peristaltic pump (Gilson, France). Recordings were made using glass electrodes (3–5MΩ; filamented borosilicate glass, Harvard Apparatus GC120TF-10, U.K.) were used containing an high K^+ solution (composition in mM KCl 150, $MgCl_2$ 2, NaH_2PO_4 1, Na_2HPO_4 8, EGTA 0.5, $CaCl_2$ 0.001 pH 7.25 with 1M KOH, osmolarity = 310mOsmol). The recording electrode was linked to a patch clamp amplifier (Axopatch 200, Axon Instruments, USA) connected to a computer running Clampex 8.0 (Axon Instruments) via an Tecmar TL1 interface (Labmaster Scientific Solutions, USA).

Cell selection was based on morphology, with emphasis on those with small to medium diameter and a smooth surface (selection based on GFP expression was not feasible as the microscope was not equipped with fluorescence imaging). The cell membrane inside the pipette was voltage clamped at a holding potential of –60mV (V_h) and then ruptured by gentle suction and a brief hyperpolarising pulse to –150mV to obtain whole-cell recordings. A voltage ramp (–150 to +100mV; V_h = –60mV; 1s) was used to determine the zero current potential (V_z) and slope conductances between –90mV and –60mV (G_{-75}) and –10mV to +10mV (G_0). A 20mV hyperpolarising pulse was applied for post hoc determination of cell membrane series resistance (R_s) and capacitance (C_m) and the membrane time constant (_). Rapid bath superfusion (300-400μL.min^{-1}) of 100μM ATP (Sigma) provided inward currents in CHO cells voltage clamped at –60mV. ATP was typically applied for a duration of 60 seconds. Chronic purinergic receptor desensitisation was assessed by repeated applications separated by wash of at least 180 seconds duration. Analysis of data was carried out using Clampfit 8.0 (Axon Instruments) as previously described[14].

Calcium Imaging

CHO cells were plated onto 5cm culture dishes which had 2cm holes drilled in their bases affixed with microscope slide coverslips treated with 1:10 Poly D-Lysine (Sigma): PBS to promote cell adhesion. Prior to imaging, cells were loaded with 4μM Fluo-4 AM (Molecular Probes, USA) diluted from a 1mM stock containing 50μg Fluo-4 AM 5 per cent (w/v) pluronic F-127 in 50μL dimethyl disulfoxide and incubated at 37°C in 5 per cent $CO_{2(g)}$ for 60 minutes before washing in PBS and reincubation for a further 30 minutes.

Imaging was carried out using an inverted confocal microscope (Zeiss LSM410 Axiovert 100TV) with bath superfusion (275-280μL.min^{-1}) via a peristaltic pump (Gilson). The Fluo-4 indicator was excited by an argon ion laser at 488nm (Uniphase, USA) and light emitted was collected by a 40x water immersion objective (NA 1.2; Zeiss, Germany) and detected at 535 ± 25nm. 400μM ATP was applied to the untransfected (control) cells and 40μM ATP was applied to both the transfected and the pcDNA3.1–$P2X_{2-1}$ and pcDNA3.1–eGFP cotransfectants for durations ranging from 32 seconds to 113 seconds. Each application of ATP was separated by washes of at least 90s duration. Analysis of data was carried out using interactive data language (IDL).

RESULTS

CHO Cell Transfection

Transfection efficiency was approximately 20-30 per cent. Specifically, using FACS at 24 hour intervals post transfection revealed the following percentages of each cell population were exhibiting green fluorescence levels above that of untransfected CHO cells; pcDNA3.1–eGFP transfectants; 34.18 per cent at 24 hours, 22.18 per cent at 48 hours and 11.98 per cent at 72 hours, pcDNA3.1–$P2X_{2-1}$ and pcDNA3.1–eGFP cotransfectants; 17.41% at 24h, 17.82% at 48h and 8.67% at 72h (See Fig. 1C). Most of the data for $P2X_{2-1}$ expression were obtained using transient transfection. In addition, CHO cells which had been selected for stable transfection using G418 were also studied. Selection for singly transfected pcDNA3.1–$P2X_{2-1}$ cells was solely achieved through G418 resistance as there was no GFP selectable marker to indicate transformation of the cell genome. Transient transfection of pcDNA3.1–$P2X_{2-1}$ with pcDNA3.1–GFP and later pcDNA3.1–$P2X_{2-1}$ with pcDNA3.1–eGFP was confirmed using FACS.

Electrophysiology

Recordings were made from a total of 46 CHO cells which, in the absence of ATP in the bath, exhibited a mean zero current potential (V_z) of –62 ± 5.4mV, with a mean electrode series resistance (R_s) of 15.8 ± 1.4MΩ and a mean membrane capacitance (C_m) of 8.7 ± 1.1pF (Fig. 1D).

Rapid bath superfusion of 100μM ATP produced inward current responses in 5/46 cells (11 per cent) with an average current response of –934 ± 416pA. Of these current responses, two were obtained in pcDNA3.1–$P2X_{2-1}$ singly transfected cells; one (I_{ATP} = –517pA) was a stable transfectant which had undergone a total of 17 days G418 exposure, the other (I_{ATP} = –1350pA) was a transient transfectant which was patch clamped 24 hours after transfection. Analysis of ATP responses with repeated applications separated by 120 seconds,

demonstrated desensitisation which was unexpected given reports of sustained ATP current responses in other $P2X_2$ expression studies[15,16]. Analysis of the current-voltage relationship (Fig. 1E) showed that the CHO cells had no intrinsic voltage-dependent conductances whereas the ATP-activated current showed inward rectification. The mean membrane slope conductance at –75mV (G_{-75}) of 1.6 ± 0.3pS was comparable to the mean conductance at 0mV(G_0) of 1.4 ± 0.4pS. Hence there was no voltage dependency. In fact, this conductance converts to an input resistance of 714 GΩ at 0mV. In contrast, the ATP-gated current was inwardly rectifying (Fig. 1E), with a slope conductance at –60mV of approximately 8nS.

The remaining three current responses were recorded from cells cotransfected with pcDNA3.1–$P2X_{2-1}$ and pcDNA3.1–eGFP and patch clamped 48 hours after transfection. The initial current responses obtained from both these cells were more slowly desensitising and thus more characteristic of the typical $P2X_2$ response[15,16]. The first cell which responded (I_{ATP} = –302pA) exhibited chronic desensitisation of the inward current amplitude with successive ATP applications separated by 180 second washes (I_{ATP} = –41, –40, –32pA). The effect of ATP-gated currents on the whole cell current potential was also recorded (mean $V_{z\ ATP}$ = –21 ± 7.0mV). The second cell (I_{ATP} = –307pA) also exhibited chronic desensitisation of the inward current amplitude with successive ATP applications (I_{ATP} = –127, –65, –49, –53pA). The effect of ATP-gated currents on the whole cell current potential was also recorded (mean $V_{z\ ATP}$ = –38 ± 17.3mV). The third cell (I_{ATP} = –708pA) also exhibited chronic desensitisation of the inward current amplitude with successive ATP applications (I_{ATP} = –208 pA).

The effect of ATP-gated currents on the whole cell current potential was also recorded (mean $V_{z\ ATP}$ = –64± 32.5mV). The overall chronic desensitisation of the inward current amplitude is shown in Fig. 1F.

Calcium Imaging

In pilot experiments, 400μM ATP induced an elevation in intracellular calcium ($[Ca^{2+}]_i$) in untransfected CHO cells after 32 seconds. CHO cells express endogenous $P2X_7$ receptors[18,17] with an ATP EC_{50} of 1252.3μM and a detection threshold of 94.6μM[17], so this result could possibly be attributed to the ATP activation of these channels and subsequent calcium influx from the external solution. ATP was then applied at 40μM in an attempt to exclude the $P2X_7$-induced response (as $P2X_7$ receptors are insensitive to ATP at this concentration). 40μM ATP produced an F/F_0 of 6.0 (Fig. 1G), which should be compared with an F/F_0 of 4.2 observed in the pcDNA3.1–$P2X_{2-1}$ and pcDNA3.1–eGFP. As 40μM ATP is below activation for threshold for $P2X_7$ receptors, this calcium response to ATP is likely to arise from endogenous P2Y receptors which have an EC_{50} of 2.3 ± 0.5 am[19].

DISCUSSION

This study showed that CHO cells could be developed as a biosensor to detect extracellular ATP. The eGFP reporter gene provides the opportunity for fluorescence-based selection of transformants, while expression of the $P2X_{2-1}$ receptor provides the facility to detect ATP release from tissues based on the activation of inward currents that can be recorded using the sensitive whole cell patch clamp technique. The existence of endogenously expressed P2Y receptors that are strongly coupled to intracellular calcium stores indicates the potential to use calcium imaging as another means of detecting ATP release in tissues, which would involve distributed imaging of a number of CHO cells scattered over the target tissue.

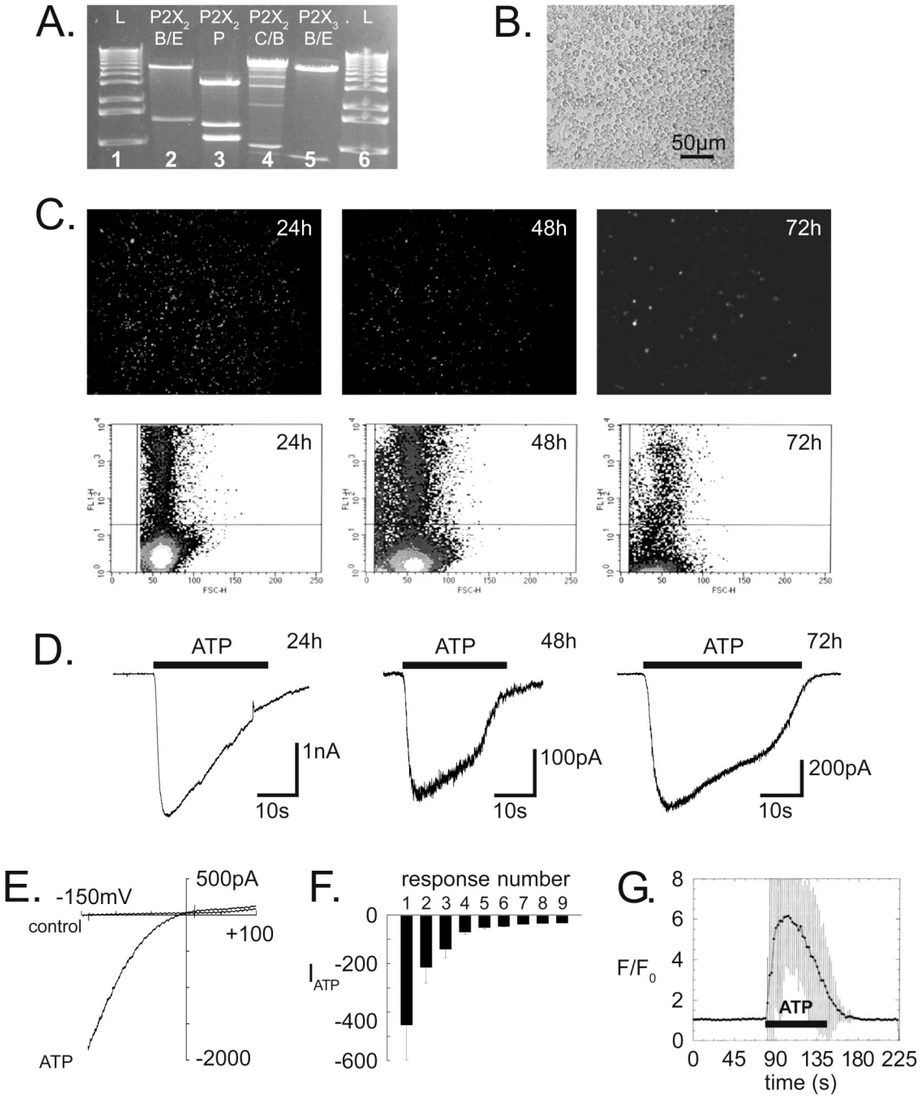
The apparent low expression rate for the both transfected $P2X_{2-1}$ protein and eGFP reporter gene as evidenced by only 11 per cent of cells displaying current responses to 100mM ATP and FACS measurements of eGFP expression showing only 20-30 per cent efficiency may be attributed to the cotransfection paradigm. Although studies exist which describe efficient CHO cell cotransfection using lipofectamine[20], studies involving GFP cotransfection of G(s) alpha cells[21] describe low transfection efficiencies (3.6±1.5 per cent) comparable to that observed here. In order to develop an efficient biosensor, the cells would need to be selected for stable transfection. Given that earlier attempts with a pcDNA3.1/NT-GFP-TOPO-$P2X_{2-1}$ chimera were unsuccessful (data not shown), future experiments could use FACS to enrich the transfected cells for G418 selection. This would then enable patch clamp recording from clonal selection to isolate cells stably transfected with both $P2X_{2-1}$ and eGFP.

Whole cell patch clamp recordings from a P2X receptor would allow the positioning of individual CHO cell biosensors adjacent to target cells within the cochlear tissue, including suspected sites of ATP release bordering the scala media. Luciferin-Luciferase assays from extracted guinea pig cochlear fluids indicate increases in extracellular ATP levels ranging from ten to several hundred nM[10] when the cochlea is exposed to stress such as hypoxia and noise stress. Given that heterologous expression of $P2X_2$ receptors generates ATP-gated currents with an EC_{50} of 1-60μM[15,22], the sensitivity of the $P2X_2$ biosensor may be insufficient to detect endogenous ATP. However, a splice variant of the $P2X_{2-3}$ receptor would provide the required detection sensitivity. Thus, CHO cells expressing P2X receptors with high nM to low μM sensitivity offer a high resolution biosensor for detection of ATP release sites in the cochlea, which would allow investigation of the mechanism of ATP release.

While there was a good correlation between transfection efficiency of the eGFP determined by FACS, and the success of whole cell patch clamp recording from the $P2X_2$ receptors, the experimental yield of only five cells out of 46 transfectants displaying ATP-gated current responses was low. Additional factors mitigating this may include the time required to translate the $P2X_{2-1}$ gene sequence, then transport and correctly assemble the resulting protein in the cell membrane. This is suggested by the ATP-induced current recordings obtained at 48-60 hours post-transfection displaying slower acute desensitisation kinetics more characteristic of the typical slowly desensitising $P2X_2$ current responses [15,24]. Although studies of P2X receptor expression in HEK 293 cells have shown a >90 per cent response rate to ATP in recordings made 12-48 hours after transfection[23]. No studies of $P2X_2$ receptor expression in CHO cells [17, 24] have reported any details on the time required after transfection to obtain functional channel expression. The successfully transfected CHO cells exhibited ATP-activated membrane conductances around 8nS. Given the reported unitary conductance of $P2X_2$ receptors in CHO cells of 22pS[16] this indicates that approximately 230 trimeric $P2X_2$ channels were correctly assembled in the cell membrane. The ability of immunocytochemistry to elucidate protein expression independent of functionality or membrane localisation provides scope for further experiments to evaluate the feasibility of a $P2X_2$-based CHO cell biosensor for ATP release in the cochlea.

Previous studies have reported the ATP EC_{50} conferred by the endogenous P2Y receptors to be in the low μM range[19]. It is reasonable to suggest that a suitable biosensor for cochlear ATP release may be developed simply from imaging the ATP induced increase in $[Ca^{2+}]_i$ mediated by these endogenous receptors expressed in CHO cells placed beneath a cochlear slice preparation from which ATP release has been induced. However, such a setup would not allow individual CHO cells to be positioned immediately adjacent to sites of ATP release and consequently the biosensor may not achieve the level of sensitivity required to detect localised fluctuations in endolymphatic ATP. There is

Figure 1



A. Multiple restriction enzyme digests oflinearised pcDNA3.1 containing either the $P2X_{2-1}$ fragment used forCHO cell transfection (Lanes 2.4) or a $P2X_3$ fragment which was used as a control (Lane 5). Restriction enzymes are as follows: B/E = *Bam*HI and *Eco*RI; P = P*vu*I1; C/B = *Cla*I and B*am*HI.

B. Bright field image of CHO cells.

C. (top row) Fluorescent images of eGFP expression in cotransfected CHO cells at indicated times of analysis following transfection; (bottom row) percentage of cotransfected CHO cells expressing eGFP. FACS analysis of eGFP expression shown as the number of cells whos fluorescence exceeded the null flouresecence levels of untransfected CHO cells (indicated by the horizontal line).

D. ATP (l00μM) induced an inward current in CHO cells expressing $P2X_{2-1}$ receptors that changed in profile over time. from a rapidly (24 h) to a more slowly desensitising current (48 and 72h).

E. The current voltage relationship of the ATP-gated current response exhibited inward rectification and reversed around OmV.

F. Repeated applications of ATP (l00μM) revealed run down in the amplitude of theATP-gated current.

G. Fluorescent Ca^{2+} imaging of ATP(40μM) induced rises in intracellular Ca^{2+} levels from ATP-gated currents and activation of endogenous P2Y receptors.

also the additional problem of run-down of intracellular calcium stores associated with P2Y receptor – PLC – IP_3 receptor-gated signalling. Thus while having potential, the feasibility of calcium imaging of CHO cells during prolonged and repeated ATP exposure would need to be investigated further. However as the pharmacological threshold and EC_{50} for P2Y receptor activation is comparable to the most sensitive of the P2X receptors, this component of the study has developed an interesting new element of the proposal to develop the CHO cell as a biosensor.

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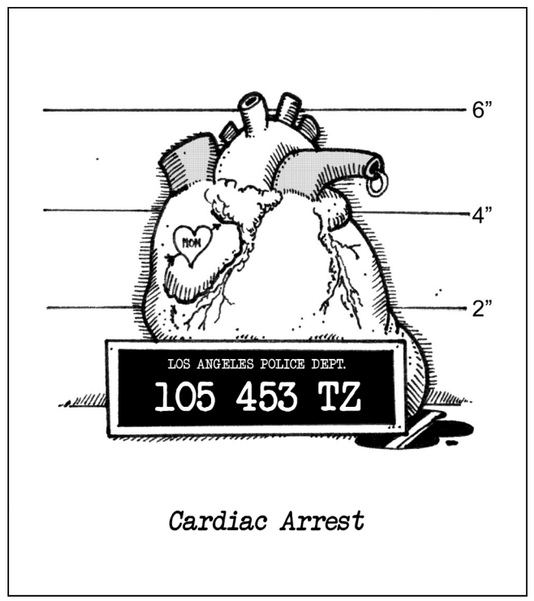

Cardiac Arrest

FEATURE : OPINION

A Fijian Experience

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The author has a strong interest in Pacific Island and indigenous health as his mother was born in Tonga. He has also been involved in student politics and education for last 3 years and is the NZMSA president for 2006. He is involved in rural health with NZMSA and Matagouri Rural Club and he was the OUMSA president in 2003/2004.

Sigatoka Hospital

At the end of fourth year in 2004, I decided to spend my summer holidays working in hospital in Fiji to gain some more clinical experience. I have always had a strong interest in Pacific Island health as my mother was born in Tonga and moved over to Auckland when she was young. I decided to work in Fiji because our family had a timeshare in Sigatoka and there was nearby hospital.

There are two main public hospitals in Fiji, one in Suva and one in Lautoka. I worked in Sigatoka District Hospital, about 1hr drive from Nadi along the beautiful Coral Coast. The Sigatoka valley is known as the "salad bowl" of Fiji because of the many crops, fruit and vegetables that are grown. These products would be on sale at the local markets along with freshly caught fish and shellfish and imported spices and curry mixtures from India. Food is an important part of life in Fiji and for a Dunedin student this was paradise!

Sigatoka District Hospital has about 60 beds, with 4 doctors, nurses and midwives. There are two separate men's and women's wards, obstetric unit, emergency surgery theatre, emergency department (ED) and an outpatient's clinic. The beauty of this set up was that I could do a bit of everything. I mainly stayed in the emergency department, where I would be with another doctor or often just with a nurse! It was a bit daunting at first to be responsible for admitting patients and their management. All I can say is that I learnt very quickly and became very good friends with the staff who I learnt much from. In Fiji, GPs are private so people either come to the ED or go to the outpatients, this meant we dealt with many people and problems that varied from trivial to life threatening.

When most people think about Fiji, they think about the resorts and lazy cocktails on the beach. After working there it soon became apparent that the reality was far different, as 25.5% of Fijian's live below the poverty line. Many Fijians live in villages in concrete or corrugated houses. Power is usually by generator, with outside showers and toilets. There are often many people living in one house. These factors impact hugely with the control of infection and disease. We would often see a whole family or part of a village for vomiting and diarrhoea. This would be related to a common water or food source. Scabies and skin abscesses were very common because of the poor hygiene, humid conditions and the shortage of water. The skin abscesses would develop as folliculitis or small abscesses and because of the reluctance to see a doctor would develop into carbuncles (large abscesses) with surrounding cellulitis. For severe cases some needed surgery. These late presentations were common with indigenous Fijians. They would normally see the doctor after they have tried herbal or local remedies. Other examples of late presentations included diabetic patients with 2 year old foot sores, dislocated shoulders that had been out for 2 months, pregnant women that had not been to any antenatal appointments and turning up the day before delivering. Fijian Indians on the other hand came more readily to the hospital. It was sometimes difficult to judge their level of pain and how sick they were. The lack of quick lab tests and reliable imaging made decisions on transferring patients to the main hospital in Lautoka very difficult.

We would often see a whole family or part of a village for vomiting and diarrhoea.

The ED was always busy, with no triage system and only 4 beds. It was hard to work out who you had and hadn't seen. We would often be rehydrating 10 patients for gastroenteritis and then mixed in between, have some very serious cases. One particular occasion in the space of 20 minutes while working with a nurse, we were stabilizing a patient for transfer with heavy vaginal bleeding, managing a patient with BP of 230/150 and then a pick up truck pulls up with a man who fell out of a large tree while pruning it! Another busy occasion when the ED was overflowing, I noticed an Indian girl, about 13 who I hadn't seen. I asked her to get up from her chair and onto the bed. She was markedly

ataxic and nearly fell over. She had marked torticollis (stiff head turned towards the right) with a left lateral gaze. My immediate impression was that she had a neurological problem. With limited resources, I did a detailed history and examination. It turned out that she had been treated with Prochlorperazine (Stemetil) for nausea and vomiting two days ago and that she was developing a hypersensitivity reaction to the medication. After consulting the pharmacist, we found out that we had to give Benztropine. Unfortunately the hospital had no more supply of this!! So we had to get her father to drive into town to a community pharmacy to buy the Benztropine. Meanwhile, the girl was getting very scared and crying. I have to admit I was feeling worried as well. To add to the situation, a priest arrived and started praying for the girl with the family. Finally her father arrived and we gave the Benztropine, which thankfully resolved things.

In the afternoon I would often work in the outpatients with another doctor. We would have very large clinics often seeing 40 plus people in an afternoon. These clinics were general medical, surgical and diabetes. Diabetes and heart disease, like in the western world, is a major problem in Fiji. We would often see patients at each clinic that had blood sugars over 35mmol! The Indian population seem to be affected just as much as the Fijian population. Public and preventive health is an area that will need to be targeted, though it is difficult to advise a sugar cane farmer who works 12 hours a day about diet and exercise!

The Fijian people have to be the friendliest people I have met. They seldom complain and are always smiling. I became very good friends with the staff and got to know many of my patients. I used to run through the villages after work and often people would yell after me "hello doctor!" or "my stomach is better now!" I thoroughly enjoyed my time in Fiji. I will hopefully do part of my elective in Tonga and I would like to go back to the Pacific Islands to help in the future.

I think every medical student should go at least once in their career to a country with limited resources. It puts your medicine in perspective. It makes you realise the resources you have, and emphasizes the importance of the basics of history taking and examination. For me the experience has made me think a lot about my career in medicine and the differences in health care in the world. I feel privileged to be part of a profession that is able to make a difference to the quality of life of many people.

I used to run through the villages after work and often people would yell after me "hello doctor!" or "my stomach is better now!"

Top: a traditional Fijian ceremony.
Bottom: a village dance on Nacula island.

FEATURE : OPINION

Leaving Banda Aceh

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Steve Tripp is a medical doctor who works for the University of Otago Physiology Department as a Medical Teaching Fellow, and as a locum House Surgeon for Dunedin Public Hospital. Steve has an interest in public health, with a particular interest in community development in the third world. He is currently planning to move to Cambodia in 2006 to work in community development.

I woke up this morning at 5AM with three mosques seemingly competing for my attention. I could swear they had crept up in the night and were directly parked outside my tent. After half an hour the Islamic prayer calls were winding down and so some Christians started up with their praise music. They had only stopped at midnight the night before! I was just dropping off back to sleep at 6:30 and there was a bloody earthquake! God, if you're trying to get my attention, can't you give me dreams and visions in my sleep! I gave up and got up.

There's something tragic about waking up in the morning and squashing a fat, bloody, mosquito on the inside of your net! Tragic for the

The day after arriving I saw the unbelievable sight of a steel hulled barge that had been picked up by the tsunami, swept over roads, houses, trees and deposited, in a suburb three kilometers inland.

mosquito that spent a happy night consuming only to find himself trapped and doomed; tragic for me, who spent the night being consumed for no ultimate purpose. I would rather make the sacrifice for a cause although the cause of mosquito reproduction is not one of my priorities. Are our causes worth more? Are our happy days consuming worth more?

I feel sad to be leaving Banda Aceh, but happy to be going home; a sense of fulfillment for what has been achieved, but also a sense that I am leaving unfinished work, a story without an ending. It has only been three months after the tsunami that claimed the lives of 140,000 Acehnese lives. It will be years before the wounds that remain can heal. Since arriving in Banda Aceh nearly four weeks ago my ideas of reality and life have been seriously challenged. The day after arriving I saw the unbelievable sight of a steel hulled barge – larger than an Olympic size swimming pool – that had been picked up by the tsunami, swept over roads, houses, trees and deposited, in a suburb three kilometers inland. I met people who had lost their entire families on Boxing Day of 2004, while I was still digesting the turkey and alcohol from the day before – and yet they knew how to laugh, to cry, and to sing. I worked with people who were so grateful to be able to do something for their neighbours, grateful to have work, and grateful that we had come to help that they would shower us with praise, food, transport, gifts and love.

On the flight to Banda Aceh nearly four weeks ago I was sitting next to a medical specialist – an eye surgeon from Jakarta – with a preference for retinal surgery over corneal surgery. "To an eye doctor, the cornea is to the retina what a wife is to a girlfriend. With a girlfriend you never know what to expect. There always seems to be surprises and you have to tread carefully. With a wife, things are predictable, domestic and, well, to be honest, boring!" And the guy is still married!

Leaving Banda Aceh today I sit next to a critical care specialist. Bahman is an Iranian, with a United States passport who lives in New Zealand. He's quite a passionate man with a passion for environmental health and a passionate dislike of George W. Bush. Over twenty years ago, Bahman left Iran because of Saddam Hussein; eighteen months ago, he left the United States because of George W. Bush. Together we had great discussions and many laughs.

Looking out of the airplane window, I see Jakarta – large, sprawling, flat and overcrowded. Until recently, it had the dubious reputation of being the largest city in the world without an organized sewage system. Having taken off from Jakarta airport fifteen minutes ago I see densely

populated areas below. This is the island of Java, where many of Indonesia's quarter billion people live.

When sacrificing our blood, sweat, and tears for a cause, I guess we can never know if it will ultimately make a difference. But we have to hope that it will. I've had to do that over the last few days especially. Even though there is no definite sign that our efforts will continue we have had to move ahead as if they will. Servants to Asia's Urban Poor, the non-governmental organization I came here with, had two objectives for our short time here. The first was medical relief work. The second, to develop and initiate a plan for long-term community development work; specifically helping the Acehnese people to help themselves – walking alongside them as they rebuild their lives.

The first goal was straightforward, immediate – responding to a sense of urgency. Working with interpreters I saw up to eighty patients a day, dispensing medications, giving advice, and listening to stories in various clinics. I also assisted in distributing food and hygiene kits, and water and sanitation provision, in order to provide minimum standards in the affected areas. Seeking to reach the more isolated areas I joined a team that traveled on one of the few remaining fishing boats to an area 7 hours down the west coast of Sumatra. There we lived for ten days, in tents with no mattresses, no plumbing, no electricity – not even Internet access or a good cafe. Living like the refugees we distributed food to, we ate fish and rice three times a day. The well water tasted salty and seemed a little too close to the latrines for my liking. It felt like a luxury when a passing boat dropped off a supply of bottled water and some Australian army food ration packs – even if they were two years past their use-by date – mmmm, Vegemite on crackers!

I saw up to eighty patients a day, dispensing medications, giving advice, and listening to stories in various clinics.

Wading through the leech infested waters on the way to Padung. There was a road and bridge here before the tsunami.

Being the only doctor at the camp presented some challenges. Along with the two nurses and the midwife who made up the healthcare team we were a versatile bunch acting as pharmacists, occupational therapists, physiotherapists and nutritionists as required. Creativity was a very valuable virtue in treating diverse illnesses with a limited range of medications and equipment and also in other tasks such as designing medication shelves (made from felled coconut trees) that could fit in a tent.

While based at this camp we moved around the area holding mobile medical clinics in areas that were isolated by the loss of roads and administrative services including healthcare. This was on top of the isolation that these areas were subjected to before the tsunami because of the civil war in this region. Not all the needs we dealt with were tsunami related and perhaps the most meaningful clinical experience I have ever had was in helping seventeen-year-old Anwar. Anwar lived in Padung, a village a few kilometers inland. For two hours we had walked, rafted and waded through leech infested waters to reach Padung to provide a mobile medical clinic. Although only just touched by the actual tsunami waters, Padung was one of the many villages that had been directly affected through the loss of roads and infrastructure. Two years ago Anwar had fallen out of a tree, broken his back and been paralyzed from the waist down. For two years he was carried everywhere. For two years he barely moved a muscle in his body. When I met him he greeted me with, "I want to walk!"

Doctors had passed by – sometimes offering empty promises of a neurosurgery referral or a CT scan – but nothing had happened. No one could provide the miracle that Anwar was hoping for. After hearing his story my first comment dashed his hopes entirely. "You will never walk again." Was I callous? I felt it. I felt irrelevant, maybe much like the doctors that had been past before. But then Anwar said, "If I can't walk, I can't work", and the full tragedy of this situation hit me. Anwar had been hoping for one sort of miracle. Restoration of what was lost. No one had helped him to work towards making the most of what he still had. There was no wheelchair. He had never even heard of one and had no upper body strength needed to use one. He was also suffering from malnutrition, urinary incontinence, and constipation, and was also covered in pressure sores from lying day and night on a hard wooden bed without being able to move himself.

We dressed his ulcers, gave advice, provided nutritional supplements and encouraged his family to build a frame over his bed to help him exercise. Within four days his upper body strength improved so that he could prop himself up in bed, roll himself over, shift his own legs, and even move around the room for the first time in two years. Meanwhile, back in Banda Aceh another miracle had occurred, someone was giving him a wheelchair. For the first time in two years Anwar could be independently mobile. Anwar will never walk but he can work. He can still be involved in his community creatively contributing in ways that are uniquely his.

The second goal – developing projects including ongoing public health initiatives, such as health education, water and latrine provision for schools, and income generating projects – was not so straightforward and required stepping out into the unknown. I had to attend meetings with government officials and develop plans as if what we hope for will happen. I operated as if we will have the people available to continue. I operated as if we will be allowed to stay. I operated as if we will have the people and resources to continue; as if we will be allowed to stay. I have shifted beyond a purely evidence-based practice to a practice that includes risk, faith and vision – and it excites me.

There were a couple of reasonable earthquakes over the last couple of days. Lying in my tent this morning at 6:30, I felt slightly nauseous with the motion of the earthquake. It gave me the feeling of floating, as if sitting on my surfboard just beyond the break. The realization hit me; we are floating. We live on tectonic plates floating on the Earth's surface. We don't have control. We spend so much of our time, money and energy in trying to gain control of the world around us, to gain for ourselves security over our own destiny.

When will we learn to seek harmony with our world – to move when she moves, to sway when she sways? Why do we continue to be confrontational, to come up against our planet in conflict, trying to overpower and subdue it? We are not in control. We are simply walking on water, floating on a sea of lava. In spite of our technology, our centuries of scientific progress, we need to acknowledge that control can only belong to a force much greater than we will ever be.

For the first time in two years Anwar could be independently mobile. Anwar will never walk but he can work. He can still be involved in his community creatively contributing in ways that are uniquely his.

Advanced Choice of Employment: Friend or Foe?

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Back in old days, the one thing that filled hearts with dread and anxiety was the fear of seeking employment as a First Year House Officer. Unsuspecting trainee interns found themselves drowning in masses of paperwork, fine-tuning their secretarial skills by writing countless letters and hiking up phone bills with calls to "all the right people". Unfortunately for some, a lack of organisation skills left them at a disadvantage in comparison to their super-efficient peers who managed to juggle their way through a nerve-racking system! That lazy streak, combined with the lack of funds and transport to travel left many Trainee Interns frazzled, dazed and confused.

Thankfully, someone somewhere decided that enough was enough, and a board was formed to dispel all this confusion and inconvenience. In 2003, a brilliant concept, known to most of us as Advanced Choice of Employment (ACE) system was introduced throughout New Zealand to handle applications for all house surgeons for the upcoming 2003/2004 intake. However, how brilliant is this scheme? Has it really eased this painful transition into the working world?

The ACE system clearly has its benefits. Firstly, this wonderfully structured system not only handles the application forms, but organises interesting events such as the annual Resident Medical Officer (RMO) Job Fair where interns can wine and dine, while looking for an ideal place to work. In addition, the invaluable information that each hospital has to offer allows applicants to make a fuller and more informed job choice. The extensive list of the various District Health Boards (DHBs) one can choose from, as well as the number of positions each has available acts as a game of eeny-meeny-miny-mo for the indecisive, and gives all applicants a clear view of their opportunity cost, and their chances of a successful employment at each hospital.

It is therefore clear that the entire job application process has undoubtedly been made easier and more user-friendly. The online form, along with an application guide, also allows applicants to review the status of their application at all times. Applicants are also saved the trouble of filling up multiple forms, as now they only have to complete one, which will be forwarded to all the DHBs. And if all that was not enough, little tick boxes are provided to politely remind most of us suffering from post-exam-amnesia about the little things we may have forgotten to include.

There is also an online Guide to writing a Curriculum Vitae (CV), which helps both the applicants put forward their most relevant and outstanding achievements, and the RMO staff by making the volumes of CVs more reader-friendly. And you thought being a Trainee Intern was difficult! Lady Luck is certainly smiling upon you, with this super-easy system, a raise of $10,000 in your grant next year, and a guarantee to be placed ahead of the New Zealand Registration Examination (NZREX) and international students who also want a peck at the pie!

The author was born in Kuala Lumpur, Malaysia in 1979 and migrated to New Zealand eight years ago. He is looking forward to beginning his career as a doctor in Palmerston North next year.

One foreseeable problem in this system is that of generic applications. However, a solution to this was devised by giving applicants the option to write their own covering letter to their hospitals of choice. This new system also provides applicants with a wide variety of DHBs available for them to apply to, which some applicants are not even aware of !

However, sceptics find themselves asking if this system is as perfect as it seems? Apparently not. Upon closer investigation, one will find that this system does have its drawbacks. Firstly, applicants who miss out on their first job choice will not be awarded their second. Instead, chances are they would end up going to a hospital fairly low down on their list. That is just purely a corollary due to the mechanism of the system. But how does this system work?

Well, it's a little complicated considering there are 300 applicants for ACE to sort through but here's a stab at a simple explanation. If you get a place in the hospital of your first choice, throw a party. If you don't, you'll probably be on the hit list for many other hospitals. But remember though, the jobs are handed out based on the priority of the students. So if you are on the list of a hospital that's your second choice, and someone else has ranked that hospital first, they are going to get a place there even though the hospital may have ranked them lower than you.

The bottom line is, a great deal of this system is based on luck. So if luck just isn't your thing, I suggest investing in some four-leaf clovers pronto! However, this cloud does have its silver lining. For those who are not too keen on the idea of spending an entire year in a place bottom on their list, word has it that the people who form the brains behind this system are working hard in trying to maintain the highest level of quality across all the hospitals through the matching system. Now that's good news!

Now let's consider why the ACE system was founded in the first place. The most logical response is to maintain justice and simplicity in applying for first year jobs, of course. But any medical student will surely know that in any given situation, the likelihood of bias will always exist. So where is the bias in ACE? When you look hard enough you are bound to find something, and from where I stand, I can see a small crack in the equitable side of things.

The people who are exposed to this bias are the non-Trainee Intern applicants, who comprise of the NZREX graduates, and international students who trained in New Zealand but who are not citizens or residents of this country.

The NZREX graduates comprise of doctors who obtained both their degrees and their training abroad in countries like India, Saudi Arabia, Bangladesh, etc. These doctors migrated to New Zealand many moons ago and were promised a job as a doctor upon arrival. Unfortunately, these promises were broken, and they were forced to take up other jobs including driving taxis, working as cashiers and setting up dairies to provide for their families. Due to this prejudice, a large group of these foreign doctors recently set up a campaign to fight for their rights as New Zealand residents/citizens, and as trained doctors whose expertise and skills are being wasted on jobs clearly outside the medical arena. The government then decided to set up a bridging programme for them to learn about the medical system here in New Zealand, and create a New Zealand Registration Examination to allow integration of these doctors into our system. After all, New Zealand has always been crying out that it has been short of doctors, what better way than this to solve the problem?

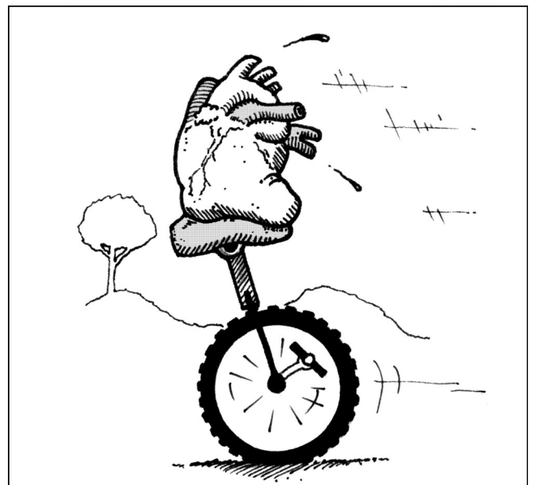
This bridging programme is good in recognising the rights of this group of educated and trained doctors, some of whom are undoubtedly brilliant, well-skilled and caring. The problem here is whether these doctors, who have been trained under extremely different conditions and who are unexposed to the New Zealand health system, can become whole-bodied, all rounded, competent doctors who are able to withstand the pressures and demands in an NZ hospital in just one year? I am sure that the NZREX programme is vital in the metamorphosis of these butterflies, but as life is, some turn out prettier than the others.

The second group of applicants, who in fact are on the bottom rung, are the international students who trained in New Zealand but are not citizens or residents of the country. They have been rigorously exposed to the fondly remembered Patient, Doctor and Society course as well as the universally loved Ethics lectures. And not to mention the exciting, invigorating talks about Maori health, which in fact, for those of you who didn't pay attention in class, is of utmost importance! They played the same games as we did, and studied for the same dreaded examinations that we did, but sadly, they were not provided with the 'Get Out of Jail Free' card.

Applicants who miss out on their first job choice will not be awarded their second. Instead, chances are they would end up going to a hospital fairly low down on their list. That is just purely a corollary due to the mechanism of the system.

Now, here comes the tricky bit. We want to protect our kind. Extremely important. That is, Trainee Interns who are New Zealand residents/citizens having the first priority. Excellent. Then come the NZREX doctors who are also residents/citizens who deserve their rights as residents in NZ. Sure. And lastly, the Trainee Interns, just like us, who don't have that stamp on their passport. Now is that fair? Being at the bottom of the pecking order means they have virtually no chance at securing themselves a job in the NZ health industry. Word has it that there are many international students who are brilliant at what they do and who definitely have the whole package when it comes to being an outstanding first year house officer. So is it really fair for us to penalise them just because they don't have a pretty sticker on their passport?

In the good old days, job hunting was about competition. He who excelled would get the best job. But in the modern world where we eradicate the tall poppies, gone are the days when being the best was everything. What is to happen to our Hippocratic Oath where we swore to put our patients first and above all, do no harm? Could there truly be a world where we maintain job equality in the face of preserving the finest optimum medical care? Could the ACE system be the key? Only time will tell.



Cardiac Cycle

Hodgkin disease in the HIV setting

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ABSTRACT

Recent studies have shown an increased incidence of Hodgkin disease in individuals with Human Immunodeficiency Virus (HIV), especially among intravenous drug users and homosexual men. These patients have a poorer prognosis when compared to non-infected individuals with Hodgkin disease. They tend to present with more advanced disease, with more unfavorable histology, and have a poorer response to chemotherapy. Highly active antiretroviral therapy may permit the use of aggressive chemotherapeutic regimens that were overly toxic in the previous era. However, relapse rates remain high. With the use of various combinations of chemotherapeutic agents, median survival in patients with HIV-associated Hodgkin disease ranges from only 12 to 18 months. Given the shared clinical features of these patients, familiarity with its presentation and early diagnosis may improve survival.

Keywords

Hodgkin disease; HIV; AIDS

Neka Dunlap completed her undergraduate education at the University of California, Berkeley where she received a BA in Psychology. While writing this article, she was influenced by an African female patient with HIV associated Hodgkin's disease who she encountered during her third year internal medicine rotation. As an African American woman in medicine, she feels that it is her duty to educate as many people as possible about the AIDS epidemic.

INTRODUCTION

The immune system is believed to play an important role in the development of cancers,[1] therefore it is no surprise that immunodeficiency increases the risk of certain types of cancers. Kaposi sarcoma (KS) and Non Hodgkin Lymphoma (NHL) are the most common malignancies associated with Acquired Immune Deficiency Syndrome (AIDS). In fact, they are considered to be among the so-called 'AIDS defining illnesses'. Although Hodgkin Disease (HD) is not part of the US Centers for Disease Control and Prevention (CDC) definition of AIDS, there is increasing evidence of an association between HD and HIV infection. KS and NHL have a much higher relative risk of development in HIV infected patients (73,000 and 165 respectively). However, studies have established an association between HD and HIV infection with a relative risk of 8.[2] More than 300 cases have been reported mainly from European countries, most of these patients being homosexual men and/or intravenous drug users.[3] Heightened knowledge among clinicians about epidemiology, symptoms, and treatment options may help improve the poor survival in these patients.

Results from cohort studies of homosexual men enrolled in the San Francisco City Clinic [4] and in the Multicenter AIDS Cohort Study [5] conveyed that Hodgkin's disease is more prevalent among HIV- infected homosexual men compared to the general population. Reports from the Italian Cooperative Group for AIDS-Related Tumors [6] and from Spanish researchers Rubio *et al.* [7] suggest that intravenous drug users were at exceptionally high risk of developing HIV associated HD. In these studies, the incidence of HD in HIV increased with AIDS diagnosis, suggesting that the probability of developing HD is proportional to the degree of immunosuppression. These studies also showed an association between Epstein-Barr virus (EBV) and HIV-HD 70-100 per cent. Although the etiology of HIV-HD remains unknown, EBV infection is seen as important in its pathogenesis.[8,9]

Clinical presentations of Hodgkin disease in the HIV setting

Hodgkin disease in HIV infected patients tends to present differently from that in non HIV infected patients. Mediastinal disease is less frequent and the disease often presents with B symptoms which include fever, night sweats, and weight loss.[10] Advanced stages (stages III and IV) at diagnosis as well as extranodal involvement are also typical in HIV positive patients.[4, 6-7,10-15] Among the extranodal sites, bone marrow and gastrointestinal (GI) involvement were commonly reported, which usually manifested itself as colicky abdominal pain and/or bright red blood per rectum. Other unusual extranodal sites in HIV infected patients include skin, central nervous system, tongue, and lung. Prognostically poorer subtypes such as lymphocyte-depleted and mixed-cellularity HD are the most common among HIV patients as opposed to nodular sclerosis which is the most common in immunocompetent patients in the United States.[16-19] In addition, HIV infected individuals present at a younger age with HD with the majority falling between the ages of 35 and 49 years compared to the bimodal age distribution observed with non HIV-infected individuals. Hodgkin disease should be thought of and ruled out in any HIV-infected patient with low CD4 counts, B symptoms, and GI complaints.

Hodgkin disease and immunosuppression

Hodgkin Lymphoma tends to be more common in individuals with low CD4 cell counts.[20] The majority of people with HIV who have developed HD have had CD4 cell counts around 200 to 300 cells/mm^3. It is therefore suggested that reconstituting the immune system with HAART will aid in controlling the lymphoma. Dr Ribera and colleagues[21] reported that patients with HIV-related Hodgkin's disease who receive HAART have a better response to therapy and improved survival compared with similar patients who have not received HAART. The Spanish researchers studied 45 patients with HIV associated Hodgkin disease. Patients were divided into two groups; those who received HAART before or started HAART shortly after Hodgkin disease diagnosis, and those who had not received HAART or started HAART after completing treatment for Hodgkin disease. The researchers found that among patients who received HAART before or shortly after Hodgkin disease diagnosis, the response rate to treatment was significantly higher than in the other group. Multivariate analysis showed that only HAART was independently associated with a complete response to treatment (odds ratio 5.3, $p = 0.026$). Both disease-free and overall survival were also significantly better among patients who had received HAART. Multivariate analysis found HAART predicted better survival in these patients (odds ratio 8.6, $p = 0.002$).

Prognosis

In non HIV- infected patients with advanced stage III or IV disease, HD is potentially curable with complete remission rates of 70 to 80 per cent with ABVD (doxorubicin, bleomycin, vinblastin, dacarbazine) and relapse-free long-term survival in 60 to 70 per cent of cases.[22] The prognosis of HD in HIV population is significantly worse by comparison. In patients with HIV-HD, complete response rates to a variety of combination chemotherapeutic regimens have ranged from 20 to 100 per cent and median survivals generally in the 12 to 18-month range.[6-7,12,16,23-24]

Treatment

The optimal treatment regimen for Hodgkin disease in the setting of HIV infection remains unclear. For advanced-stage disease, ABVD was shown to be superior to chlormethine, vincristine, procarbazine, and prednisolone therapy (MOPP) in freedom from progression in two trials[22,25] and in overall survival in one trial.[26] Table 1 contains chemotherapeutic combinations and outcomes reported in HIV positive patients with Hodgkin disease. For those individuals with severe immunocompromise, consideration may be given to dose-modified standard regimens. Autologous hematopoietic stem cell transplantation and granulocyte colony-stimulating factor (G-CSF) has been determined safe and effective when used adjunctively with chemotherapy. Both methods help rebuild the immune system by replacing cells that are killed during the course of drug treatment.[24,28]

CONCLUSION

Recent studies suggest an elevated incidence of Hodgkin Disease in the setting of HIV when compared to the HIV negative population. The presentation and prognosis of HD differ greatly between HIV-infected and non-infected patients. Because the prognosis in HIV associated HD is poor, familiarity of how it presents and early diagnosis can help improve the survival. Although various treatment regimens have been studied, data regarding the most efficacious combination are still lacking. As the incidence rate of HIV infection remains steady and people are living longer with the disease, research on concomitant infections and malignancies in the setting of HIV specifically are becoming more crucial.

Table 1. Summary of treatment and outcomes in studies of HIV associated Hodgkin's disease

Reference	Sample size	Chemotherapy	CR[1] (%)	Median Survival (Months)
6	21	MOPP[2] alone or MOPP/ABVD[3]	65-MOPP/ABVD 46-MOPP alone	15
23	17	Epirubicin, vinblastin, & bleomycin	53	11
24	21	ABDV and G-CSF[4]	56	18
27	20	Stanford V[5] plus antiretroviral therapy	80	18
29	12	BEACOPP[6]	100	Could not be calculated

Key to Table 1

CR Complete Remission

2 MOPP chlormethine, vincristine, procarbazine, and prednisolone

3 ABVD doxorubicin, bleomycin, vinblastine, and dacarbazine

4 G-CSF granulocyte colony-stimulating factor

5 Stanford V mechlorethamine, doxorubicin, vinblastine, vincristine, bleomycin, etoposide, and prednisolone

6 BEACOPP bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisone

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Telemedicine: rural health and beyond

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Rural health care: a global problem

In a recent televised open debate program in Nepal, people from Achham, a remote district, complained that a doctor was at service in their district hospital for hardly 6 months in the last 6 years. The Public Service Commission of Nepal, which is responsible for the recruitment of doctors in such governmental hospitals, never gets enough applicants in the first place and the situation gets progressively worse with every further step such as the examination and appointment to the vacant posts at such remote hospitals. The country has seen a significant increase in the number of medical graduates after the 1990 re-establishment of democracy but there is still a lack of doctors in rural hospitals.

Is the number of doctors serving in rural areas only a problem of developing countries? No, every country is facing this problem, the difference being only of magnitude. The geographical distribution of doctors is skewed towards urban areas in every country. In India, about 75 percent of modern (allopathic) medical practitioners are concentrated in urban areas[1], which cover 27 percent of the population. New Zealand also has the problem of retaining health care workforce in rural areas despite their enviable environment. The strain on the practitioners who remain threatens to compromise the availability and quality of the services they provide.[2] Even the United States of America is not free of such problems. Rural America has 20 percent of the nation's population but less than 11 percent of physicians.[3] Similar to the scenario elsewhere in the world, the smaller and the more remote the place, the more difficult it is to attract and retain physicians in the USA.[4]

Developed countries like the USA and UK have partially solved the problem by recruiting doctors coming from developing countries in rural areas, but this has cost more to rural health of developing nations. To overcome the disparities in health care of rural people due to geographical barrier, telemedicine has been developed as a new system of health care.

Telemedicine: a promising solution

WHAT IS TELEMEDICINE?

Telemedicine is the delivery of health care services, where distance is a critical factor. Health care professionals use information and communication technologies to exchange information relevant to diagnosis, treatment and prevention of disease and injuries, research and evaluation, and the continuing education of health care providers. This is all in the interest of advancing the health of individuals and their communities.[5]

A BRIEF HISTORY OF TELEMEDICINE

Telemedicine has long been practised in one form or another, but in the real sense the development of telemedicine occurred in NASA's manned space flight program. "Telemedicine is really an outgrowth of the space program", as said Daniel Johnson former president of AMA[5]. During the early stage of manned space program NASA's scientists were concerned about the physiological ill effects of zero gravity on astronauts' vital functions. They developed a telemedical system to monitor vital functions in the astronauts (telemetry). Telemedical capabilities for diagnosis and treatment of medical emergencies, establishment of health maintenance systems and biomedical experimentation developed as the space program needed longer flight time and orbital stations.[7] Then, being virtually out of the scene for some time, telemedicine resurged in the 1990s because of rapid expansion of information and telecommunication technologies. Telehealth and telemedicine have become the WHO strategy for achieving equal healthcare for all since 1997.[8]

HOW DOES TELEMEDICINE WORK?

Telemedicine basically works using information and communication technologies in various forms and for various purposes. And accordingly are the services it provides.

- *Teleconsultation*: General Practitioner or any trained health care worker in the rural area transfers the patient's data, including images, through the Internet to an expert (consultant) for a second opinion. The expert, based on the information, can make diagnosis and write a prescription for the patient and relay it back to the patient. Through video conferencing, live interaction between the two parties can be organized and the health care worker can elicit the required information and perform examination of the patient as per the need of the expert.

- *Teleradiology*: In a rural area, specialist opinion can be sought from an expert radiologist in a city by transmission and display of digital radiological images. These include x-rays, CT scan and MRI images.

- *Telepathology*: Similar to the concept of teleradiology, here the histopathological diagnosis is made by an expert seeing the digital image of the slide sent via the internet.

- *Telehome nursing*: It is mostly applied to the patients suffering from chronic illness, in place of the traditional home visits. Here the patients are monitored and nursed from distance away while they are at home using electronic devices to measure the clinical parameters and advised via videophone.

- *Telesurgery*: Telesurgery is probably the most amazing development made possible by the modern day technology. Success in this regard came in 2001, when surgeons in New York performed

cholecystectomy of a 68-year-old woman in Strasbourg, France using remote-controlled robots and a high-speed cable video link.[9] This procedure was expensive as it used especially designed fibre-optic link. To make it cost effective in 2003 surgeons in Canada performed telerobotic assisted antireflux surgery using regular national internet system with a special priority networking connection that allowed information signals to travel along the public information highway, but in a lane blocked off for its private use to avoid traffic jams.[10]

• *Telehealth*: Sometimes used interchangeably with telemedicine, telehealth includes a diverse group of health-related activities for distance learning in health care delivery settings for both health professionals and patients. This also encompasses the use of information technology in public health, research and administration of health services. The health care worker in the rural set up can get updated with the recent development in the field of medicine with online resources like journals and research databases. Nowadays, telehealth is also known by the names online health and e-health.

Beyond boundaries

Telemedicine can run beyond national geographical boundaries and bring the concept of a global health care village into reality. People from developing countries can benefit from the clinical expertise in developed countries. and developed countries can get services like teleradiology and telepathology from well accredited doctors in developing countries at a significantly low cost, which is made possible only through the use of the internet. The developed countries can also benefit from the medical expertise in the developing countries. In September 2003, Dr Ashok Sethl, Chief of Interventional Cardiology at Escorts Heart and Research Centre, New Delhi, demonstrated angioplasty procedures live via a satellite link to an annual meeting of heart surgeons in Washington, D.C. [11]

Telemedicine has created a global debate as to whether it can provide health care to disadvantaged rural people or not. There are, on one side, enthusiasts of telemedicine who envision the potential in telemedicine to put an end to the present disparity in health care service to rural areas, whereas others are of the opinion that it is not perfect solution to the present problem and may even do harm to the development of local resources. The enthusiasts argue that telemedicine helps to redistribute knowledge and expertise to rural areas in a cost effective way. There is evidence that telenursing can be cost effective, electronic referral and teleconsultation can be cheaper, and teleradiology, which is widely used in the USA, is found to be safe and in right circumstances economical.[12]

However, some people think that telemedicine is going to affect the traditional doctor patient relationship and argue that it can impair the clinician's decision-making. There are the issues of maintaining confidentiality, guidelines of practice to ensure safety and standard and legal issues, which are still not perfectly clear in the case of telemedicine. There is fear that the use of teleconsultation through a local clinician on a larger scale may stifle the development of local resources and lead to dependence. The remote consultant may prescribe treatment not knowing what is available, affordable, or acceptable locally.[13] The establishment cost and maintenance of the service can be a great challenge to run telemedicine in remote rural areas of developing nations where there are either no, or intermittent, power supplies, and phone lines are unreliable.

Richard Wooton, currently the editor of a specialised peer reviewed journal of Telemedicine and Telecare, once expressed concern that commerce might become the driving force behind the spread of telemedicine.[14] Still, many people fear that telemedicine is market driven, with technological push (and associated big commercial interest) being greater determinants in its development than the clinical pull.

CONCLUSION

Telemedicine is unlikely to ever be as good as face to face consultations.[15] However, owing to the constraint of human resource and time, telemedicine helps greatly in delivering health care service to deprived people of rural areas worldwide, and educating the health care professionals and patients in much better way than what has been practiced conventionally.

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FEATURE : CONFERENCE REPORT

The 2005 Annual Scientific Meeting of the Australasian Society of Aerospace Medicine and the 5th Asia Pacific Congress of Aerospace Medicine

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The 2005 Annual Scientific Meeting of the Australasian Society of Aerospace Medicine (ASAM) and the 5th Asia Pacific Congress of Aerospace Medicine convened at the Gold Coast International Hotel in Surfers Paradise, Queensland, Australia from the 15th to the 18th September 2005. It was hosted by the Aviation Medical Society of Australia and New Zealand (AMSANZ; www.amsanz.org.nz), Australasian Society of Aerospace Medicine (ASAM; www.asam.org.au), and the Asia Pacific Federation of Aerospace Medicine Association (APFAMA). Delegates were compromised mainly of doctors, who were Designated Aviation Medical Examiners (DAME), aerospace medicine researchers including a large delegation from the Chinese Society of Aerospace Medicine, members of the aviation industry and representatives from the military.

Aerospace medicine is the medical specialty that is concerned with the interaction between the aviation and space environment and human physiology, psychology and pathology. All medical practitioners need to know something about aerospace medicine because everyone who flies experiences some form of decompression related alteration in physiology. Ninety percent of people who fly get Jet Lag (fatigue), oedema, or microvascular venous failure. The remaining ten percent experience asymptomatic Deep Vein Thrombosis (DVT), symptomatic DVT, Pulmonary Embolism (PE) or, very infrequently, death. In our lifetime, space tourists may present with orthostatic intolerance (hypotension associated with fluid shifts).

Themes of the conference included aviation psychiatry, aeromedical operations and space physiology. Research presented included plans for artificial gravity during interplanetary missions, vestibular-oculomotor deficits experienced by astronauts post-flight (Space Adaptation Syndrome) and the related spatial disorientation during shuttle landings (which result in 70 percent of landings rated as poor including one being near catastrophic), mental stress and cardiovascular variability in student airline pilots, aeromedical evacuation operations in Banda Aceh, and anti-SARS experiences in China.

The impact of fatigue in the aerospace industry was the main focus of the conference. Professor Philippa Gander from Sleep/Wake Research Centre at Massey University and Dr John Caldwell from the US Air Force were the keynote speakers. Fatigue is physiologically induced by increasing the number of continuous hours of wakefulness and sleep loss. Circadian factors are also important and cause the body to perform like an orchestra during the pre-performance tune up. Fatigue is already a significant problem in the aviation workplace given long periods monitoring automated systems and, with respect to aircrew, changes in time zones and the length of flights. Fifty percent of military pilots, 71 percent of corporate pilots, and 80 percent of commercial pilots admitted that they had fallen asleep or nodded off in the cockpit during flights. It is therefore not surprising that the 3 - 7 percent of all aviation accidents that are recorded as fatigue-related is considered to be just the tip of the iceberg.

Fifty percent of military pilots, 71 % of corporate pilots, and 80 % of commercial pilots admitted that they had fallen asleep or nodded off in the cockpit during flights.

Sixteen hours of continuous wakefulness is required to induce serious behavioural detriments similar to alcohol intoxication. Specifically restricted sleep causes:

- irritability
- degraded alertness
- slower reaction time
- poor psychomotor skills
- slower cognitive processing
- cognitive fixation
- less creative problem-solving
- immune suppression
- increased appetite (for junk-food)

The problem of fatigue is about to get significantly worse with the introduction of 24/7 operations and the development of ultra long haul passenger aircraft making 22-hour commercial operations from Sydney to London non-stop. Currently 16-hour flights operate from Singapore to Los Angeles. Military flights have been up to eighteen hours but pharmacological intervention is routine. Studies have shown F1-17 pilots can be kept awake for 2-3 days with no statistically significant loss of function when given amphetamines every couple of hours.

Sleep restriction is common in the aerospace industry (as it is for medical students and junior doctors in hospitals) and there is large individual variability in sleep and resistance to the effects of sleep loss. Recovery is based on deeper more consolidated sleeps and not hour for hour reparation. After two uninterrupted sleeps, EEG indicates the normal sleep architecture returns. However, it takes more than three days before full waking function is restored. Sleep needs to be maximised prior to work and during lay-overs and the rest opportunities during flights needs to be maximised. Commercial pilots use hypnotics (such as Temazepam) to assist in reconstructing the sleep architecture but sleep medications are not recommended for ongoing fatigue.

Courses in aviation medicine are offered at the Wellington School of Medicine, University of Otago. Papers include aviation physiology, aircrew and performance, airport and travel health, and clinical aviation medicine. For further information see:

www.otago.ac.nz/Web_menus/Dept_Homepages/aviation

REFERENCE

Asleep in the Sun
Conference Handbook
The 2005 Annual Scientific Meeting of the Australasian Society of Aerospace Medicine and the 5th Asia Pacific Congress of Aerospace Medicine

FEATURE : BOOK REVIEWS

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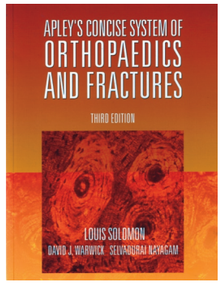
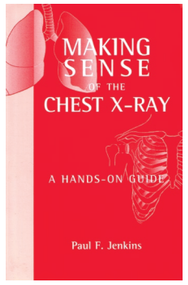




Illustrated Clinical Anatomy
Abrahams, Craven and Lumey, $89.00

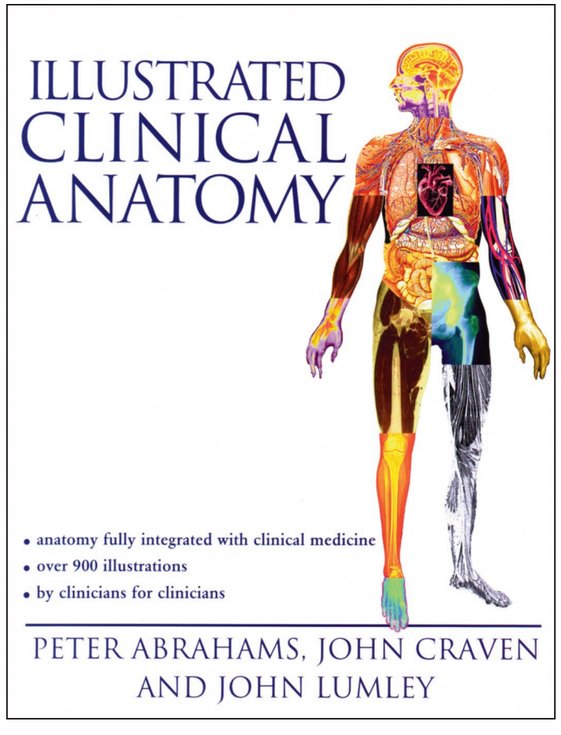
This anatomy textbook describes itself as "…integration of anatomy teaching with the study of clinical medicine". It has been written by two surgeons and a GP, also a professor of clinical anatomy. I like the sound of that. Doctors writing for doctors-in-training.

At first sight I thought it was too small to be an anatomy textbook, being about half the size of Moore. However in my brief read I found this to be no problem. The layout of Abrahams *et al.* is as is normal for anatomy textbooks: by body region. However there is one difference that seems just what I've heard some many people say they wanted. It's logical. For example, in 'The Pelvis' the bones are first discussed, followed by joints, muscles, fasciae and organs. Function is described throughout. An aspect of this book that I particularly like was that the clinical information was not in a box to the side. It is in the text itself, and highlighted. I would expect such things form a 'Clinical Anatomy' textbook.

I would also expect cool pictures. Some of the clinical photos are quite graphic – like some guy casually sitting with a sternal puncture, or a right indirect inguinal hernia extending into the scrotum. They don't just have photos though. There are lots of diagrams, imaging and surface anatomy. A patient won't come to you partially dissected (hopefully). This book has many photos of a person with the relevant organ/area superimposed. It helps with perspective and tying all our disjointed anatomical knowledge together.

Another good aspect is the one page of SAQs and MCQs at the end of each region. And there are answers, thank goodness.

In summary, I liked it. However, I wouldn't replace an atlas with it, there isn't enough of that sticky detail. I would like the anatomy department to have a look and see if it covers all that we need to, the anatomical and the clinical. Appropriate for all levels of medical training.



Making Sense of the Chest X-ray: a hands-on guide
Jenkins, $70.00

The lecturer says "and you can see clearly that this man has a bronchiogenic cyst". You look enthusiastically at the projected image, and see no difference between that and the primary tuberculosis patient's x-ray. What to do?! It would be wonderful to have an experienced physician at hand to lead you through the complexities. Paul F. Jenkins may be your man.

His book begins with a systematic approach to interpreting the radiographs. He refers to this many times and the final section of the book challenges you to diagnose patients using the method. Within the body of the text are five chapters focusing on specific features, such as "Consolidation, Collapse and Cavitation". The radiographic appearances are explained and pathologies detailed. For example, within the "Consolidation" part of the chapter is "What is the distribution of the abnormal shadowing?" given below are the possible causes of each type of distribution. This would be a wonderful tool for differential diagnosis.

'Making Sense of the Chest X-ray' is a well written book. It is as though Dr Paul himself is speaking to you. There are little text boxes throughout containing clinical associations, warnings and "pearls of wisdom". Abbreviations are explained at the beginning. My need for bullet points was well satisfied. However the names of diseases, syndromes and the likes made things a bit tricky. What on earth is Osler-Rendu-Weber syndrome? Because the book requires higher medical knowledge and is so clinically focused I feel that it would be best suited to clinical-years students and junior doctors. However, a pre-clinical student with a few textbooks and a radiographic inclination would also reap wisdom from Jenkins' guide through the murky chest x-ray.

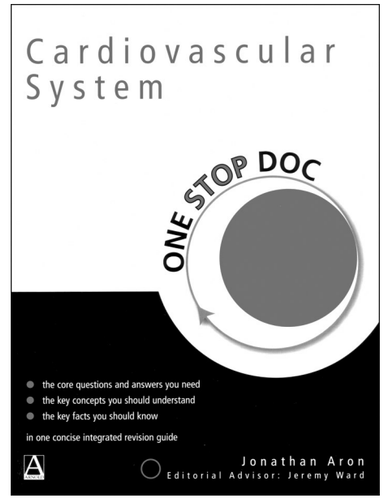
Apley's Concise System of Orthopaedics and Fractures, 3rd edition
Solomon, Warwick and Nayagam, $85.00

This textbook aimed to introduce medical students and trainee surgeons to modern orthopaedics, with a focus on "actual diseases". The authors also wished to provided guidance on simple procedures without excessive detail. Knowing how to operate – now that sounded exciting.

They didn't lie. After going through the pathogenesis, clinical presentation and imaging, for example, the treatment was discussed. If treatment included surgery you are briefly told of the goings-on in the operating room. And focus is definitely on the disease/injury/condition. One thing I found was that conditions were discussed in different ways, sometimes the differential diagnosis was detailed and sometimes not, for instance.

The layout is reasonable. Again there are the wee boxes containing condensed and important information. The book is structured by general orthopaedic stuff, conditions by body regions, and one section on fractures and joint injuries. At the beginning of the chapters the subjects contained are listed with page references. This would be very handy for quick reference. However, I found it slightly difficult to 'jump into' and pick out certain things. It is quite hard to see where a new condition begins and if you're looking at a new subject or just a subheading. Furthermore, you really need to know your anatomical terms: "…by pressing on the dorsum while manipulating the wrist into flexion, ulnar deviation and pronation". Saying that, there are lots of pictures, MRIs, diagrams, and funky clinical photos.

I would say this is worth the cash if you are really interested in becoming an orthopod. For orthopaedic training I would suggest something with more detail. There is a bigger book 'Apley's System of Orthopaedics and Fractures', which is said to have more detail in descriptions and in surgical procedures.



One Stop Doc
Series of nine, various authors, $44.99 each

Well now, 'One Stop Doc' sounds like medicine made easy. I was curious. On the front of each of the nine books there is a statement that it will cover the core questions, the key concepts and the key facts. And that it is an integrated revision guide. I hadn't seen anything like this for medical students.

The books contain questions on anatomy, physiology, biochemistry and pharmacology. Questions are in the form of True/False, short answer and multiple choice. Many questions are based on cases. Oh and the answers are written really tiny at the bottom of the page facing the questions. On that page also is the gem of this series: a concise and easily read explanation of the answers. One other nice thing is that the abbreviations are not only clarified at the front of the book, but also on the bottom of the pages that contain them.

These are truly revision tools. I wouldn't base my entire respiratory system knowledge on the information given on the 'explanation page', for example. However, they are very good. A bit on the pricey side at $44.99 a head. Have a look for yourself if you can and see if you think they're worth it.

The series consists of:

- Nervous System
- Cardiovascular System
- Respiratory System
- Musculoskeletal System
- Gastrointestinal System
- Endocrine and Reproductive System
- Renal and Urinary System and Electrolyte Balance
- Metabolism and Nutrition
- Cell and Molecular Biology

Urgent government funding needed for rural curriculum

Xaviour Walker
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Jesse Gale
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New Zealand currently faces a shortage of rural doctors.[1,2] In recent years we have seen both our medical schools and the government make efforts to address this problem. A recent review[3] found that there were four main factors at the undergraduate level that promote rural recruitment and retention:

- Selecting students of rural origin
- Teaching and placements in rural locations
- A curriculum with a primary care emphasis
- Other student support such as rural mentorship and rural health student clubs

In 2004 the government created 40 additional funded places in our medical schools for students of rural origin (i.e. with schooling or other significant life experience in towns of under 20,000 people). Overseas studies show that students with rural backgrounds are more likely to pursue careers in rural medicine.[3,4] However,"rural recruitment requires far more investment than simply a change in the medical school selection process."[5] As indicated above, another crucial aspect will be the provision of high quality undergraduate medical education in rural settings and with a primary care emphasis.[3] Curricular changes such as these are also important for developing a vertically integrated career pathway for rural practitioners.

Teaching medicine in rural locations is more expensive than in centralized urban teaching hospitals. Additional funding is required for the infrastructure and support that students need on rural attachments, such as transport, accommodation, distance teaching technology, and rural general practitioner reimbursement. There is at present no specific government funding of rural undergraduate curricula in New Zealand medical schools. In 2004, the medical faculties of Auckland and Otago submitted a proposal to Government for $12 million to fund a twelve month rural curriculum for the rural origin students and a twelve week rural attachment for all students. The full funding was agreed to, and promised in 2004, but has not been delivered.

There is presently a successful and popular seven-week rural GP placement existing at Dunedin School of Medicine, but it is at risk of termination due to funding constraints. This course is enjoyed by students for the practical skills, clinical contact, and community involvement, and students who had never considered rural practice have changed their attitudes following this course.[6] It is also popular because the essential student support (e.g. accommodation, transport, technology, supervision) are provided by the university and rural stakeholders. The communities and rural doctors themselves benefit from the relationships with students and the medical schools. Rural practice offers not only experience in the primary care, but also extends to secondary and lower tertiary level care. However, the rural programme at Dunedin School of Medicine is operated on a tight budget and depends upon the generosity of many rural general practitioners. Without extra funding from government, even this seven week course is at high risk of being removed from the curriculum.

The New Zealand Medical Students' Association (NZMSA) supports the development of a fully funded twelve month rural curriculum. The NZMSA will work closely with the universities and other stakeholders of rural health.The NZMSA believes there is a lot of good to be gained from rural medical education - for students, the communities they work in, the rural workforce, and New Zealand as a whole. For rural education to be successful, it must be a positive, well supported experience for students and their rural teachers, and this will require additional funding.

Rural medical education represents an investment in the health system, as well as education. The rural community is an integral part of New Zealand, and deserves health care equity. The rural origin students are entering their fourth year in 2006. Without government funding, our medical schools cannot deliver a rural curriculum. We must convey this sense of urgency to government to deliver this funding.

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The Patient Flow Project: what impact has it had?

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ABSTRACT

As the New Zealand population grows, so too does the demand for health care. Health care providers must service as many people as possible while operating on a limited budget and with limited resources. In June 2002, the Canterbury District Health Board commissioned the *Patient Flow Project Report*,[1] the recommendations of which were later piloted and implemented in May 2003 at Christchurch Hospital. This initiative focused on increasing patient throughput while maintaining an acceptable standard of care. Among its policies was the aim to maximise hospital bed utilisation, and two of the tools used to achieve this included a reduced Average Length Of Stay (ALOS), and early morning discharges. This summer studentship conducted a small-scale literature review to analyse international methods for managing patient flow, and investigated concerns that the increased flow afforded by the *Patient Flow Project* would manifest itself in preventable readmissions, declining patient satisfaction and higher workloads.

KEYWORDS

Patient Flow Project; patient throughput/ flow; Average Length of Stay (ALOS); readmission; discharge planning; patient satisfaction

INTRODUCTION

The changing nature of hospital care to accommodate increasing demand is becoming apparent with a more dominant presence of management organisations in the health care system. One such initiative employed at Christchurch Hospital is the *Patient Flow Project,* which has adopted some of the policies practiced in other countries following their success in better meeting patient demand.

In the United Kingdom the National Health Service (NHS) Modernisation Agency has earned a reputation for its innovative solutions,[2] which appear to get results. It seems the crux of their approach in aiding the NHS deliver effective health care is to provide *"the right skill at the right time in the right place".*[3] Hence their proposals often involve whole systems analyses for identifying and rectifying potential bottlenecks to patient flow.[2] Similar tactics have been employed in hospitals in the United States upon the recommendation of the Clinical Advisory Board in Washington DC[4]. Here the focus is on maximising the use of currently available resources. Future expansion of resources may increase capacity, which may meet demand, but in the meantime increasing patient flow appears to be the most effective way to do this.

Courtney Hore has an interest in Maori Health and hopes to become more involved in this field having enjoyed her first Summer Studentship last year. Courtney feels the exposure she gained to the public health system and its limited resources this early in her medical career was extremely valuable.

The *Patient Flow Project's* key objectives include admission to the correct ward, early morning discharge, discharge planning for provision of support following discharge, and improved communication between health providers. In line with these objectives the aims of the studentship were to review acute medical activity, gauge patient satisfaction, and to report on any associated impact. The preliminary findings may form the basis of future investigations.

METHODOLOGY

Two types of data were analysed; quantitative data and qualitative data.

Quantitative Data

Two data sets of acute medical activity were compiled and processed by Emendo Limited[5] from January 2002 – November 2004. The raw data was sourced from the Patient Management System (PMS), which records patients' movements through the hospital.

The data sets and the specialties included were:

- The General Medicine ward data set:

  General Medicine, Dermatology, Infectious Diseases, Immunology, Gastroenterology, and Rheumatology, (and weekend Otolaryngology activity).

- The Cardiology/Respiratory ward data set:

  Cardiology, Endocrinology, and Respiratory.

Patient flow and key trends were then investigated with consideration for:

- **Average Length Of Stay (ALOS):**
The average length of time spent in hospital. This may enable some insight into the level of burden on hospital resources, which can vary considerably amongst different specialties.

- **Readmission rates:**
The number of patients discharged and readmitted to the same specialty / for a similar condition within: 24 hours, 7 days, 30 days or 60 days. The extracts of graphical representation of this data from the summer studentship depict readmission rates within a 60-day period. These graphs give an overview of the total readmission rate, which is useful when making comparison between and within the data sets. Admission after a 60-day period decreases the likelihood that the presentation is related to a previous admission.

- Comparison of **Total Number of Discharges** and **Total Readmission Rate.** This involves evaluating whether there has been a disproportionate increase in the difference between the total readmission rate and the total number of discharges. If this were the case, ie. the disproportionate increase being attributable to a significant increase in the total readmission rate, it may suggest that the policies of the *Patient Flow Project* to promote early discharge are to the detriment of patients.

- Comparison of **ALOS** and **Total Readmission Rate.** Not only may this comparison give some indication of how the aim to reduce the ALOS per patient has impacted on readmission rates, it may also allow some prediction of the subsequent burden on hospital resources and how this has changed following the implementation of new policies like the *Patient Flow Project.*

Occupancy rates and 'outliers' (patients admitted to wards other than their home ward following an absence of beds) were also monitored and analysed in the final report[6].

Comparing trends between the two data sets may only indicate progress in the relative areas observed, as acceptable standards have not yet been established for specific specialties.

Qualitative Data

Patient satisfaction data comprised 173 inpatient satisfaction survey comments from July 2003 to June 2004. This information was collected and processed by the Corporate Quality and Risk Office at Princess Margaret Hospital. The data was further analysed to identify common perceptions of the quality of care received.

The comments from inpatients admitted and discharged from the following specialties were analysed:

- General Medicine
- Cardiology
- Respiratory

It is possible that this method of data collection would not yield results representative of the entire patient population. Those patients responding may have communicated extreme opinions allowing for bias in the resulting analysis. The data analysis required identification of common concerns. Views and attitudes for the feedback did not always communicate clear feelings of satisfaction/dissatisfaction and did not involve numerically graded responses.

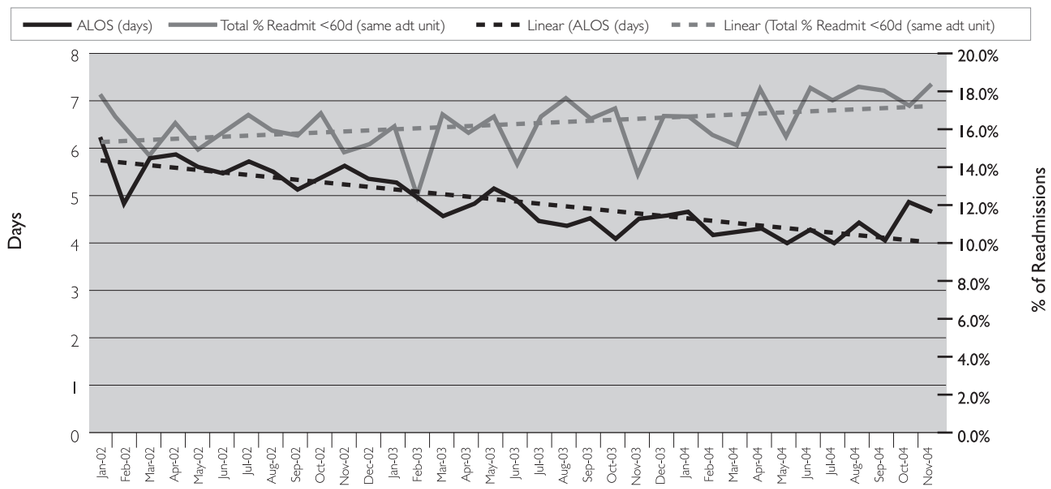
RESULTS

Quantitative Data

ALOS

The ALOS in General Medicine decreased from 5.80 to 4.00 days per patient, while in Cardiology/ Respiratory it increased from 3.95 to 4.05 days per patient (Figure 1). Hence there appears to have been a greater effect in General Medicine. It must be noted that comparing individual values may be misleading as what may be deemed progress for one specialty may be inappropriate for another.

Figure 1: General Medicine, Dermatology, Otolaryngology, Infectious Diseases, Immunology, Gastroenterology & Rheumatology ALOS vs % of Readmissions



READMISSION RATES

The total readmission rate in General Medicine increased by 0.05 per cent per month on average to give a total rate of 17.2 percent (Figure 1). However, when compared with the total number of discharges there was no relative change in the difference between their individual rates of increase. In Cardiology/ Respiratory the total readmission rate remained constant at 15.6 per cent, and when compared with the total number of discharges it had decreased ie. there was a decrease in the difference between their individual rates of increase. Cardiology/ Respiratory had a lower patient throughput than General Medicine did, and hence if patient throughput were to increase in this area the readmission rate may no longer decrease.

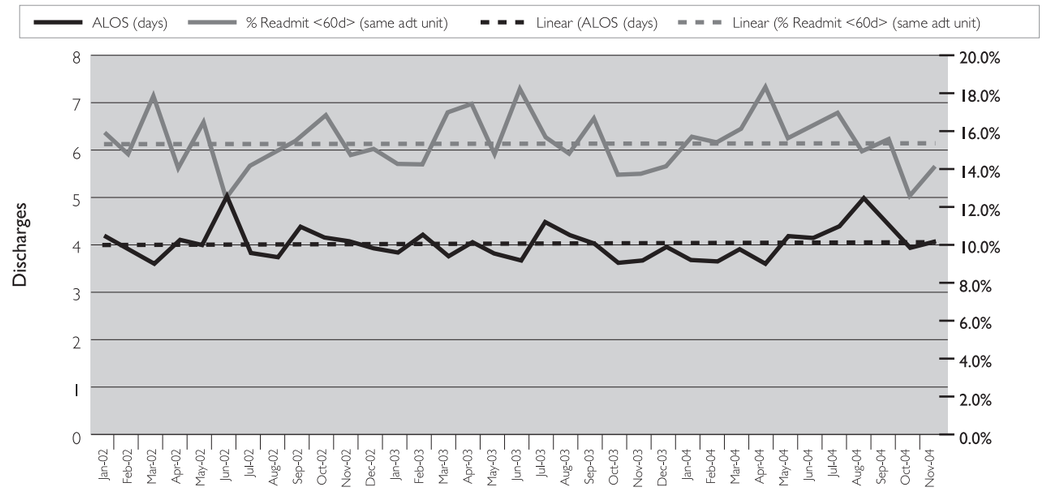
GENERAL MEDICINE WARD DATA SET: COMPARISON OF ALOS AND TOTAL READMISSION RATE

While there has been a slight increase in the total readmission rate there has been a dramatic decrease in the ALOS.

CARDIOLOGY /RESPIRATORY WARD DATA SET: COMPARISON OF ALOS AND TOTAL READMISSION RATE

Figure 2 illustrates the marginal increase in the ALOS and the consistency of the total readmission rate. While there has been a slight increase in the total readmission rate there has been a dramatic decrease in the ALOS.

Figure 2: Cardiology, Respiratory & Endocrinology ALOS vs % of Readmissions



Qualitative Data

Patients did not demonstrate specific knowledge of the *Patient Flow Project.* Some felt their short stay impacted negatively on the quality of care received as staff tried to accommodate more patients. Several patients commented on the lack of discharge planning and the long waits endured.

GENERAL MEDICINE WARDS

Overall patients commented on receiving professional and attentive service. Other patients were not quite as satisfied. There were several comments expressing disappointment over the lack of information given upon discharge, and distress over the eagerness to vacate hospital beds, and complete hospital discharges. Some patients acknowledged the high workloads for staff, but also felt this inhibited them from providing adequate care.

"You were there when we needed you and we were very impressed with the service and care we received. My husband was admitted immediately via A&E. They were terrific."

"She (the Doctor) told me to go back to the hospital, but staff were in such a hurry to get rid of me so they could have the bed I couldn't face it."

CARDIOLOGY / RESPIRATORY WARDS

Several patients praised staff for their organisation, efficiency, attentiveness and skill. Other patients felt communication was lacking between staff during changeover, between staff and patients during their stay, and throughout the discharge-planning process. Several patients were unhappy with the duration of the discharge process, and were distressed by the constant movement between beds in order to accommodate other patients.

"I experienced happy, smiling people around me. A feeling of a strong team working together with calmness and great organisation when busy. The one thing I do struggle with is on the day I left I was asked to sit in the lounge or in an armchair so that the bed could be changed. The bed then remained empty for the following three hours at which time I was picked up by family. There were times when I would have appreciated being able to lie down, especially as I had an hour's journey to get home."

DISCUSSION

ALOS

The differences in the trends identified in the two data sets may be explained by differences in the acuteness of patients presenting at the relative specialities, thus allowing for overestimation/ underestimation of the ALOS. Another possibility is that the *Patient Flow Project* is influencing the differences in the respective trends as it was introduced in different specialties at different times. It was first introduced in May 2003 in General Medicine and data collection began in June 2003 and in Cardiology/ Respiratory in October 2004. Other data on patient flow, prior to June 2003, has been and still is being collected and stored in the Patient Management System (PMS). Hence it is possible to make comparisons between the two data sets over the past three years, however there is not as much specific data on patient flow relating to the *Patient Flow Project's* policies in Cardiology/Respiratory. It may still be useful to make such comparisons to see what effect the project has made in one area, where it has been in practice for longer. The trends observed were evident before June 2003, but any initiatives taken to maximise patient throughput are bound to have had some impact in this area.

READMISSION RATES

The total readmission rate in General Medicine increased, while it remained static in Cardiology/ Respiratory. It is unclear whether these trends are directly related to the *Patient Flow Project's* implementation and the timeframe in which this occurred.

COMPARISON OF TOTAL NUMBER OF DISCHARGES AND TOTAL RE-ADMISSION RATE

The fact that there had been no relative change in the readmission rate in General Medicine suggested the efforts to reduce the ALOS and increase patient throughput were not to the detriment of patients. In Cardiology/ Respiratory the relative decrease in the total readmission rate suggested the increased patient throughput was again not to the detriment of patients. While this appears to be a more desirable outcome the level of patient throughput had not increased to the same extent as in General Medicine.

COMPARISON OF ALOS AND TOTAL READMISSION RATE

In General Medicine the ALOS decreased by a greater factor than the total readmission rate had increased. In Cardiology/Respiratory the ALOS had increased marginally, but overall both the ALOS and the total readmission rate appeared constant. As previously noted, the reduced ALOS in General Medicine did not appear to increase readmissions. Cardiology/Respiratory appeared to have an ideal outcome, but this might change should the patient throughput be increased or the ALOS decreased. If more patients may be treated adequately and without a greater chance of readmission this may be a desirable outcome from the perspective of patient flow management.

Future efforts to designate specialty-specific targets for the ALOS and readmission rates may improve the usefulness of such data analyses. In this way both patient flow management staff and medical personnel could monitor such progress.

Qualitative Data

EFFICIENCY AND EFFECTIVENESS OF MANAGEMENT SYSTEMS

In general patients did not demonstrate knowledge of the Patient Flow Project but commented on some of its related policies. This suggests that the relationship between the policy changes and patients' satisfaction may not be completely applicable. Several patients recognised the effort to reduce the ALOS with the majority of patients equating a shorter length of stay with a reduction in the quality of care provided. Patients were aware of changes made to discharge procedures and highlighted particular concerns regarding the length of the discharge process. This might be an area in which to improve the efficient use of resources, and the standard to which discharge procedures are completed. If deciding to discharge patients and initiating discharge-planning procedures was done before 11AM, patients might feel better informed and prepared. This would also enable patients to organise transport and make arrangements with caregivers without experiencing unnecessary delays. The Patient Flow Project already has policies regarding discharge planning, however these have not yet succeeded in diminishing the waiting period between informing the patient of their eligibility for discharge and their actual discharge.

CONCLUSION

The general conclusion has been that while patient flow has increased this has not occurred without some compromise. Quantitative data analyses demonstrated that relative to an increased number of discharges the total rate of readmissions had not significantly increased. Qualitative data analyses of patient satisfaction suggested there was a general lack of knowledge amongst patients surrounding the *Patient Flow Project's* policies. Patients were unhappy with the reduced lengths of stay they experienced and the lack of discharge planning. At the same time many patients acknowledged the demands placed on hospital staff and were happy with the quality of care they received.

THE FUTURE OF PATIENT FLOW MANAGEMENT

It is inevitable that there needs to be new initiatives to manage patient flow, as a response to the increasing demand for health services. There are many ways in which current procedures could be improved, such as by following the recommendations outlined in our final report .[6]

Future expansion of resources may increase capacity, which may meet demand, but in the meantime increasing patient flow appears to be the most effective way to do this.

ACKNOWLEDGEMENTS

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continued from page 13

Obesity Epidemic (continued)

We designed and carried out a pilot study assessing the amount and type of advertising and shops within a 1 kilometre radius of 10 secondary schools in the Wellington (urban) and Wairarapa (rural) regions. The schools were chosen both to represent an urban/rural difference as well as the extremes of socio-economic status (SES). Schools were only included if they were situated in neighbourhood environments, i.e. those in central business areas and totally rural areas were excluded. Information about type, product, size, distance, category etc was collected. One of the most important aspects of the study was developing a system to classify advertisements as 'healthy' or 'unhealthy,' using the New Zealand 'Food and Nutrition Guidelines for Adolescents'.[11] What we found was that overall there were a total of 1408 outdoor advertisements around the 10 schools, and 61.5 per cent of these were for food. Of these advertisements, 70.2 per cent were for 'unhealthy' foods. There were more food and more 'unhealthy' advertisements in higher SES areas; however food advertisements were on average closer to schools in lower SES areas. The three major categories of food advertisements were soft drinks (21.6 per cent), frozen confectionary (16.2 per cent) and savoury snacks (11.4 per cent). The majority of the advertisements were associated with dairies, in fact on average there were 22 advertisements on dairies and only three on other outlets. There was an average of 224 outlets around each of the 10 schools, of which 56.3 per cent primarily sold food and 67.9 per cent sold some food. Furthermore food outlets were on average closer to schools than other outlets. Rural neighbourhoods had a lower proportion of food stores. The most common outlets were dairies and takeaway stores, each making up 14.7 per cent of the outlets.

Despite the pilot nature of the study, it has provided some initial information about the prevalence and relatively 'unhealthy' content of food advertising in secondary school neighbourhoods. The next step is to carry out a nationwide large-scale study to better place outdoor food advertising into a context of total food advertising exposure. However, these findings provide tentative support for responses by policy makers to reduce aspects of the 'obesogenic' environment in order to stem the obesity epidemic.

So what can be done? Possible directions may follow the path of tobacco laws in the United States by creating safe zones around schools.[12] Currently the economics of food promotion far outweigh those of health, since it is estimated that for every $1 spent by the World Health Organization on trying to improve nutrition, $500 is spent by the food industry promoting processed foods.[5] So, regulations (or even taxes) could be used to shift the balance of advertising towards 'healthy' foods. Indeed, advertising need not be always negative as it has been major force for improving some aspect of the New Zealand diet (e.g. industry marketing of olive oil). However, a co-ordinated approach needs to be taken to ensure that further controls in just one area (e.g. outdoor advertising) does not lead to ballooning of advertising in other areas (e.g. television and internet advertising).

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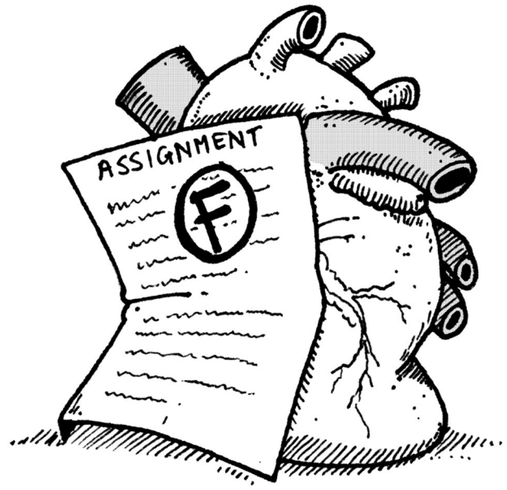

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