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The Editorial Committee proudly presents to you, Volume 4, Issue 1 of the Medical Student Journal of Australia (MSJA). This year we have chosen the theme “Sui generis” which, in its Latin translation means “of its own kind”. Our journal, inherited from its strong yet humble beginnings as a population health project in 2009 continues from strength to strength. This year the MSJA has embarked on a bold process of expansion that will, in future editions, see this journal include all year levels on the editorial board as well as increasing the number of accepted allied health manuscripts.

The Editorial Committee of the MSJA strongly believe in the philosophy that early exposure to research in medicine fosters a career of lifelong learning and encourages the pursuit of research. Indeed, a strong research focus early on in one’s career builds a clinician committed to providing evidenced based clinical practice with the greatest benefit to the patient. This is achieved through students actively engaged in the process of expert peer-review and the editorial cycle, giving them a bona-fide experience of submitting, editing, re-reviewing, and publishing a quality manuscript. Volume 4 Issue 1 has been blessed with the support of expert reviewers from a number of disciplines. These reviewers are world-renowned clinicians and researchers, who, in addition to providing timely support and advice to our authorship, ensure the highest quality of the submitted manuscripts.

Through the process of producing Volume 4 Issue 1, The MSJA editorial committee have made significant advances to expanding the readership of the journal. For the first time we have advertised our journal to students of allied health, as well as international students from the immediate Asia Pacific region. We believe that a peer-reviewed student journal is an important medium through which health students from Australia and the Asia Pacific can share advancements of their fields of study, thus inspiring interprofessional learning and communication. Indeed, the MSJA is fortunate enough to have been invited to present at the annual conference of the Australian and New Zealand Association of Health Professional Educators in Rotorua, an experience which we hope will encourage deans and medical education staff of various colleges throughout Australia and New Zealand to encourage their students to submit their research to our journal.

On a closing note, we hope that you enjoy the scholarship within this edition. We encourage you to read our articles, and consider how you can contribute to the growing field of student-led research, and the rapidly expanding reputation of the MSJA. In particular, we encourage you to read the two articles submitted by our invited guest authors, Professor Patrick McGorry and Dr Simon O’Connor. We hope that their stories and anecdotes of life inspire you to future success.

Kind Regards,

The Editorial Committee
Volume 4 Issue 1, 2012
Reflections on a career in medicine

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In some ways, launching into a medical career was rather simpler when I began at the University of Sydney as a first year medical student in 1973. I came straight from school in Canberra and was only 17 years old. Applying for a place involved writing the name of one’s preferred faculty on a form and posting it. There were no interviews or aptitude tests.

The course was very different from what you experience now. We were the last of the six year undergraduate course and were not allowed near a patient until fourth year (which began half way through third year). We had subjects such as comparative morphology, embryology, biology, biochemistry and histology. There was a certain consistency and tradition about these subjects. Someone in our year had his father’s histology notes from 1947 and was able to follow the lectures which were identical word for word.

Graduation seemed impossibly far off to us in first year, but it happened and I began work as an intern at the Prince of Wales and Prince Henry Hospitals in Sydney. There had been a recent improvement in the working conditions, and resident medical officers were now paid for overtime (though in some places, the pay went down after hours to 3/8 time). Before this, there was no overtime payment and hospitals rostered everyone on all the time. We had night and weekend rosters in addition to our forty-hour week. I can remember terrifying weekend shifts in casualty – staffed by two interns from 8am on Saturday morning until 8am on Monday, when we went back to our usual ward jobs. We were allowed to try to sleep on a trolley in the ward, but I can remember feeling too anxious to sleep. I counted eight changes on nursing shift during a weekend on. There was in fact plenty of supervision available, if one was brave enough to wake up the registrar. Although these long shifts were frightening, and probably dangerous, they did mean a lot of exposure to acute medicine and meant that we learnt to make decisions on our own.

After a couple of years of resident work, I drifted into physician training. The Royal Australasian College of Physicians (RACP) first part exam (there is no second part) is one of the most difficult specialist exams in the world. This is the exam you must pass to begin training in a medical specialty. The college believes that all physicians should have a thorough grounding in general medicine. As a result, the pass rate for the exam when I sat it was about 30% and is now about 50%. Nick Talley and I were registrars at Prince of Wales and together spent long hours practising short and long case techniques for the exam. It took us a few goes to pass, and by then Nick had accumulated a very comprehensive set of notes. It was his idea to turn these into Examination Medicine, a book for physician trainees. Although this was not a big number of people, we felt that every one of them would buy any book that might help. This book has been very successful (to our surprise) and is used by many people other than physician trainees.

Nick and I found ourselves as registrars at Royal North Shore Hospital a few years later. I was a Cardiology registrar and Nick a Gastroenterology trainee. Instead of doing our ward rounds, we sat down together and began the first, rather primitive, version of Clinical Examination. There was no medical student physical examination book set out in a systematic way at the time. I felt it was important that a book of this sort should have some concealed jokes. I do not think Nick really approved, but then he was not usually able to spot them and they have remained in place.

We have both moved around since then, and I am now a Cardiologist at The Canberra Hospital. Nick is Pro Vice Chancellor of the Newcastle Health Sciences Faculty and President-Elect of the College of Physicians.

I think any career in medicine is interesting, and although things are changing, you all have exciting prospects in front of you. My wife who is in General Practice thinks it must be boring working in a specialty, and although on some days when I have seen five patients with palpitations in a row, I agree with her, on the whole work is very enjoyable. Cardiology for example, has changed out of recognition since I was a medical student. Our treatments are now based on large clinical trials and make an enormous difference to our patients’ outcomes. Interventional treatment is immensely satisfying. Patients, who would once have been watched as they had large myocardial infarcts, are now often treated immediately with angioplasty and recover completely. They often spend only two or three days in hospital, compared with more than a week in the past. The mortality rate has continued to decline.

Apart from responding to constant nagging from our publishers to write new editions to our books, I have had time to teach medical students and registrars, and act as a member of the National Examination Panel for the RACP.

I hope you enjoy your lives as medical students – it seems all too brief in retrospect.
I come from an Irish family with many doctors. My maternal great-grandfather was a doctor, and his daughter, my grandmother, became a doctor in her forties and worked in Dublin, outback WA, and Zambia. My father became a doctor after his brother had died as a young hospital doctor from meningitis in 1924. My dad was a chest and public health physician who looked after young men dying of tuberculosis in the 1930’s and 40’s, and later coal miners disabled by pneumoconiosis and silicosis. There was consequently much expectation that I should also do medicine, though I was initially not that keen, preferring the humanities. I studied at the University of Sydney in the heady days of the Whitlam government when idealistic and radical ideas were the currency of debate and everything seemed possible. I was attracted to psychiatry because the plight of people with mental illness was such an obvious social injustice and the system of mental health care so crude and primitive, stuck in the 1890’s. It was an aspect of health care crying out for reform and the anti psychiatry movement was impressive and extreme, yet very much in harmony with the times. Weighing all this up, I decided initially that I couldn’t consider psychiatric training because one would have had to become part of an unacceptable system, though I noted even the iconic R.D. Laing had done so!

At the end of my medical degree I couldn’t wait to return home to Newcastle where I had completed high school, and became an intern at Royal Newcastle Hospital, overlooking beautiful Newcastle beach in the heart of the city. Living in the residents’ quarters was very special. Surf addicts like myself were able to carry out on call duties sitting on a surfboard in front of the hospital. If we were needed a towel would be hung out the window and we would know we had to catch the next wave in! Sometimes though, it was torture gazing out at perfect surf on a ward round. Royal Newcastle was a unique culture in many other ways. Set up on egalitarian and socialised medicine principles by Dr Chris McCaffrey, it was led by a wonderful array of staff specialists and it provided a comprehensive inpatient and outpatient service to Newcastle before Medibank. The morale and bond between staff and the community was something I have never seen anywhere else before or since. Perhaps I am far too sentimental and nostalgic, but to me it represented a medical version of Camelot. I met my wife to be, Merilyn, who was a physiotherapist at RNH, and together in 1978 we set out on a prolonged overland “hippy trail” trip through Asia and then a one and a half year sojourn in the UK during which I completed UK physician training. I returned as a medical registrar and thoroughly enjoyed working in diabetes with Paul Moffit, a rough diamond and visionary physician. However while I had been away, the new medical school had been established at the University of Newcastle. A post graduate training scheme in psychiatry had been established, headed by a warm and charismatic Foundation Professor in Beverley Raphael, quite a different persona from the harsh and oppressive stereotypes and psychobabble I had previously been exposed to. Beverley encouraged me to give psychiatry a go. I had to run the gauntlet of numerous colleagues from professors of medicine to fellow registrars trying to talk me out of it, telling me among other things that I would be “wasting my life and career”. I recently asked a group of trainees if this experience had happened to them. I was shocked to hear that indeed in most cases even today colleagues had tried to dissuade them. Stigma and prejudice lives among doctors!

The training program was superb though the settings we trained in were characterised by disgraceful neglect and, despite the heroic efforts of most clinical staff, there were some appalling and at times illegal behaviors. Patients were heavily overmedicated, there were few psychosocial interventions, and violence and physical abuse of patients by some nursing staff was not uncommon. These experiences made me determined to play a part in changing this and bring mental health care out of the 19th century into the modern world. Deinstitutionalisation has made this possible, however, as any current medical student knows, there are still huge challenges and people with mental ill-health still get a second class service in our “mainstreamed” health system, especially in emergency departments and inpatient units. The struggle on their behalf must continue and it needs a new generation of generals, and not only people entering psychiatry for “lifestyle” reasons.

I saw academic psychiatry as an attractive option to bring about change and when Bruce Singh, one of the academics in Newcastle was made a professor in Melbourne in 1984, I accepted his offer to spend time there establishing a schizophrenia research unit at Royal Park Hospital where the inspirational discoverer of lithium, Dr John Cade, had been the superintendent. We decided to focus on first admission cases with psychosis, a crucial decision that enabled me to see that treatment for these mainly young people was delayed, traumatic, one-dimensional, and while it helped to a degree, produced a range of iatrogenic effects. The latter included the demoralising and often fatal effect of pessimism and stigma conveyed by beliefs about outcome in schizophrenia and being surrounded by large numbers of much older severely disabled and disturbed patients. We knew we had a great deal of work to do.
but we had to create optimism, a holistic treatment model with evidence-based psychosocial treatments, moderate the over-use of medication, help the devastated families, and above all intervene earlier to maximise recovery. We also knew we needed to escape from the psychiatric hospital setting!

Since then blending clinical and academic roles, though demanding, has served me very well. A steady growth of government, philanthropic and competitive grant support has enabled my colleagues and I to create first a comprehensive clinical service and research centre for early psychosis (EPPIC), a more comprehensive specialist youth mental health model (ORYGEN) which promotes early intervention and partly bridges the chasm between the traditional child and adult mental health services, and more recently Headspace, the national system of enhanced primary care for young people, aged 12 - 25 years, with mental ill-health. I have been fortunate to have worked with a superb leadership team from several disciplines over many years to reinvent and regenerate our approach, each time becoming more ambitious in our goals. Many other parts of the world are embracing these reforms and new ways of thinking. Naturally there has been a lot of resistance to change from vested interests with parts of the psychiatry field, a sign that real change is occurring! Mental health is better understood among Australians than ever before and we have good political support to move forward.

In general however I believe psychiatry is struggling in terms of attracting sufficient numbers and the right kind of people. The challenges are enormous clinically, in research and in leading and reforming the mental health system, which has become stagnant and over-regulated in so many areas. We need gifted, determined and talented clinicians and academics. Yet the settings for training are often not attractive, though many new options are becoming possible e.g. Headspace centres. We need a truly inspiring undergraduate training experience and magnetic rather than repellent early clinical ones. More role models are needed but many have found the grind of our neglected public mental health system too much for them. Nevertheless, the situation is hugely more auspicious than 30 years ago and the missing ingredient is a new phalanx of idealistic and effective leaders, people of talent and with a gift for responding to distress and mental ill-health, to ensure that when Australians experience mental ill-health they have the same access and quality of care as when they experience physical illness.
INTRODUCTION

Laparoscopic adrenalectomy (LA) has become the procedure of choice for resection of functional and non-functional adrenal tumours (1,2). Retrospective comparative studies and case series suggest the advantage of LA compared with open adrenalectomy (OA), regarding its decreased requirements for analgesics, minimal morbidity, improved patient satisfaction, shorter hospital stay and recovery time (3-5). Its success is probably not surprising, given that LA very closely parallels the widespread popular laparoscopic cholecystectomy in its avoidance of upper abdominal incision, with both procedures benefiting from the magnification and clarity of view provided by the laparoscope, and both most commonly performed for benign pathology involving small, easily dissectible tissues (6). Also, adrenal pathology appears to be well suited for laparoscopic removal, due to low incidence of malignancy, small size and associated morbidity from OA.

Functional adrenal adenomas secreting cortisol and aldosterone less than 12cm in size are among the most common indications for laparoscopic surgical removal of the adrenal gland (7). The majority of LA is performed due to hypertension arising from hypersecretory adrenal disorders such as Cushing’s syndrome and disease, aldosteronoma and phaeochromocytoma. Other indications for LA include adrenal cysts, myelolipoma, adrenal haemorrhage, paraganglioma and adrenal tuberculosis (2). Absolute contraindications include tumours greater than 12cm and symptomatic phaeochromocytomas during pregnancy, whilst relative contraindications are morbid obesity, previous surgery with post-operative scarring due to intra-abdominal adhesions (8-10). However, the use of LA for the excision of malignant lesions remains a controversial issue, and oncological outcomes between OA and LA are similar, as metastases of the gland tend to be small and confined to the capsule (11). The advantages of LA compared with OA adrenalectomy necessitate a cost comparison. Jacobs et al. compared 19 complete LA unilateral adrenalectomy and 19 unilateral complete OA and found that the average hospital cost for LA was less than the average cost for OA (7). The mean central supply charge was higher in LA than in OA, which were related to the cost of single item laparoscopic instruments during the operation (7). The aim of this study was to examine our hypothesis that LA had greater clinical and cost effectiveness than OA over a 30 year period.

METHODS

This was a retrospective study composed of all patients who underwent unilateral or bilateral LA or OA at The Canberra Hospital between January 1980 to December 2010, who had available medical records.
The study design was reviewed and approved by the ACT Health Human Research Ethics Committee (ACTH-HREC).

**Surgical approach**
The approach of the surgical procedure for adrenalectomy varied considerably between patients over the 30 year study period. The marked variation in the surgical approach was likely to be partly due to patient demographics, as well as changes in technology and improved surgical skills. In total, 59 OA (67%), 27 LA (31%) and 2 LA converted to OA (2%) were performed.

For OA, a laparotomy was performed and the abdominal organs packed and retracted away from the adrenal. On the right side, the liver and distended gallbladder were retracted superiorly, duodenum and Inferior Vena Cava (IVC) retracted medially and the fascia incised over to the right of the IVC. On the left, the spleen was mobilised and together with the splenic flexure of the colon, the spleen and pancreas were retracted infero-medially. Dissection of the fatty tissue was then performed and adrenal vein isolated and ligated before the arterial supply and the adrenal gland was excised. A check for malignancy and adequate tumour clearance was performed. Haemostasis was then obtained and the peritoneal defect closed. Suction drain was often inserted before closing the wound in layers.

For LA, the patients were placed in the lateral decubitus position and 3-5 trocars used. Generally on the right side, the triangular ligament of the liver was incised and liver rotated antero-medially. Dissection was performed until the anterior and lateral surface of the IVC was exposed. Suprarenal veins and arteries were ligated after further dissection of the fatty tissue around the adrenal gland. On the left side, the spleen was mobilised medially and then the spleno-renal and spleno-phrenic ligaments incised to medialise both spleen, and tail of pancreas as well as colon. This allowed the exposure of the left adrenal gland, and then the suprarenal arteries and veins were separately ligated and divided and the adrenal gland was taken off its bed exposing the left cura of the diaphragm. For both sides, there was a check for macroscopic malignancy and adequate tumour clearance was made, the adrenal gland was placed into an endo-catch bag and removed through one of the sub-costal ports. Haemostasis was secured by insertion of closed suction drain and closure of all wounds for the skin.

**Analysis of data**
The following data were collected: demographics, including age and gender, operative indications, year of operation, type of adrenalectomy, operative time, estimated blood loss, post operative complications, post operative length of hospital stay and hospital costs including operation cost, bed stay cost and total cost.

Data were collected in a retrospective fashion in all patients by review of the medical records provided by Clinical Records Integration System (CRIS). The operative time was defined as time from the commencement of first incision after anaesthesia had been applied to completion of skin closure, estimated blood loss was obtained from the registered nurse theatre report and anaesthesia record and the length of stay was provided by the discharge summary defined by the number of days in the hospital after the operation. Hospital costs were obtained from the Diagnosis Related Group (DRG) provided from the financial management branch of the hospital and expressed in 2010-2011 Australian dollars, adjusted for inflation. The DRG provided data pertaining to operation costs, which included (i) labour costs (surgeons, anaesthetists, anaesthetic nurses, recovery nurses) and related on-costs for all these personnel and (ii) Non labour costs (Pharmaceuticals, laundry, IT software and leasing costs, stationery, equipment depreciation). As we were not able to obtain specifically which medical and surgical supplies were used in the operating rooms on individual patients, the cost of the operating room medical and surgical supplies were purely based on an average of all adrenalectomy procedures. Thus, an operation that took two hours was costed twice the medical and surgical supplies of an operation that took one hour. Bed stay costs included general ward costs (nurses and related oncosts, laundry), ward consultations by doctors, critical care costs (doctors, nurses, laundry, pharmaceuticals), pathology, imaging and pharmacy (excluding pharmaceuticals use in operation room or intensive care unit), and allied health. For both operation and bed stay costs, they also included overheads, such as finance, human resources and other corporate management services, food services, sterilising services, property, management and maintenance, security, biomedical, cleaning, wardspersons and patient safety and quality unit. The total cost per patient, as provided by DRG was calculated by aggregating the two components:

\[
\text{Average Operating room cost per minute} \times \text{length of operation} + \text{(Bed day cost per day} \times \text{hospital length of stay)}
\]

Data were analysed on Microsoft Office Excel 2007 and are expressed as mean ± standard deviation. Statistical analysis was performed using analysis of variance using Student t test, and a p value less than 0.05 was considered to represent a statistically significant difference in outcome.

<table>
<thead>
<tr>
<th>Side of adrenal</th>
<th>Laparoscopic (n=27)</th>
<th>Open (n=61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>11 (41%)</td>
<td>28 (46%)</td>
</tr>
<tr>
<td>Left</td>
<td>16 (59%)</td>
<td>31 (51%)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>0</td>
<td>2 (3%)</td>
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<table>
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<th>Gender</th>
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<th>Open (n=61)</th>
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</thead>
<tbody>
<tr>
<td>Female</td>
<td>13 (48%)</td>
<td>29 (48%)</td>
</tr>
<tr>
<td>Male</td>
<td>14 (52%)</td>
<td>31 (52%)</td>
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</table>

<table>
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<th>Age (yr) (mean ±SD)</th>
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<th>Open (n=61)</th>
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<tr>
<td>Range</td>
<td>24-88</td>
<td>19-82</td>
</tr>
<tr>
<td>51.8 ± 16.9</td>
<td>54.3 ± 16.0</td>
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</tr>
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</table>

Table 1. Demographic data of adrenalectomy patients
mechanisms.

RESULTS

The demographic data of the 88 patients are listed in Table 1. There were 27 LA and 61 OA procedures.

A total of 90 adrenalectomies in the 88 patients were performed over the 30 year study period, comprising 80 total (89%) and 10 (11%) partial adrenalectomies. There were 47 left adrenal gland (53%) 39 right adrenal gland (44%) and 2 bilaterals (3%), comprising 45 males (51%) and 43 females (49%). On average, OA was indicated for larger tumour size (58.6mm ± 35.8) than LA (41.1±18.3) (p < 0.01). The median age of the 88 patients for adrenalectomy was 52.4 years (range: 19-88 years). The distribution of adrenalectomy patients in each decade of life is shown in Figure 1. The greatest numbers of adrenalectomy occurred when the patient was in their sixth decade of life.

OA was performed via a variety of incisions whilst LA was performed by a transperitoneal lateral decubitus approach (Table 2).

Indications for adrenalectomy are illustrated in Figure 2. The most common indication was adrenal cortical adenoma (n=29) which were either cortisol (n=10, Cushing’s Syndrome), aldosterone (n=5, Conn’s Syndrome) androgen secreting tumour (n=1) or unspecified (n=13). Phaeochromocytoma (n=23) were also common, characterised by hypertension and elevated urinary catecholamines, as well as secondary deposits (n=12) of renal cell carcinoma, non small cell lung cancer, hepatocellular carcinoma or of unknown site origin.

LA had increased operative time, but decreased blood loss, postoperative stay, complications and overall cost. Perioperative and postoperative parameters are listed in Table 3. All adrenalectomies were successfully completed by experienced endocrine surgeons. The mean operative time for combined unilateral and bilateral LA was 168±SD60 minutes compared to unilateral and bilateral OA, which was 153±SD68 minutes (p=not significant). Two procedures required bilateral adrenalectomy, both performed by OA. The longest LA was 329 minutes performed after a diagnosis of right phaeochromocytoma, whilst the longest OA was 397 minutes, due to an initial suspicion of spread of retroperitoneal tumour to left adrenal gland.

Mean intra-operative blood loss was significantly less in LA (231ml ± 243ml), compared to OA (542ml ± 658ml) (p < 0.04). The range of blood loss for the LA was 50-1000mL compared to 50-3000mL for OA. The patient of 3000mL blood loss following OA was operated with left adrenal cortical adenocarcinoma with extensive lymphovascular invasion and also required lymph node dissection. The mean postoperative hospital stay in LA was 5.5 days with a range of 2-22 days, which was significantly less than 9.9 days in the

![Figure 1.](image.png) The number of patients who had undergone adrenalectomy related to age group N=88.

<table>
<thead>
<tr>
<th>Open</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcostal Incision</td>
<td>20</td>
</tr>
<tr>
<td>Midline Incision</td>
<td>13</td>
</tr>
<tr>
<td>Loin Incision</td>
<td>4</td>
</tr>
<tr>
<td>Transverse Incision</td>
<td>4</td>
</tr>
<tr>
<td>Thoraco-abdominal Incision</td>
<td>2</td>
</tr>
<tr>
<td>Paramedian Incision</td>
<td>2</td>
</tr>
<tr>
<td>Rooftop Incision</td>
<td>2</td>
</tr>
<tr>
<td>Retroperitoneal Incision</td>
<td>2</td>
</tr>
<tr>
<td>Posterior Incision</td>
<td>1</td>
</tr>
<tr>
<td>Lumbar Incision</td>
<td>1</td>
</tr>
<tr>
<td>Flank Incision</td>
<td>1</td>
</tr>
<tr>
<td>Unspecified</td>
<td>5</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Laparoscopic</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral Decubitus</td>
<td>27</td>
</tr>
</tbody>
</table>

Table 2. Type of open as well as type of laparoscopic adrenalectomy and number of patients. N=88.
OA with a range of 5-22 days (p<0.01). Regarding postoperative complications, they were more numerous in OA (16%) compared to LA (11%) in total. Pulmonary complications were most common and only evident in the OA group (4.9%), most commonly severe cough and dyspnoea; however one patient also suffered left lung collapse postoperatively. In another patient, the IVC and renal clips failed with significant blood loss (850mL) and it necessitated a conversion from LA to OA. In addition, 2 patients who underwent left adrenalectomy via OA and LA respectively incurred injuries to the spleen, and the LA patient also had injury to the large bowel, severe wound infection and hematoma.

Regarding hospital charges, the mean operation cost for LA was $A13,156 ±SD 5065.06, which was higher than the mean charge of $A12,396 ±SD6252.41 for the OA (p= not significant). In comparing the mean bed stay costs postoperatively, the mean charge for LA procedure was $A9,630±SD7142.62, which was less than the mean cost of $A17,289 ± SD6736.86 following OA (p < 0.01). Taken together, the mean total cost for LA was $A22,785 ± SD 8652.32, which was significantly less than the mean total cost charged through OA of $A29,684 ±SD10026 (p = 0.02) (Figure 4). In calculating mean operation costs and mean bed stay costs, they were inclusive of items such as direct and overheads, salary and non-salary expenditure, diagnostic tests, pharmaceuticals and depreciation.

**DISCUSSION**

OA has a number of advantages, including wide exposure of the operative field, easy exploration of the peritoneum and contralateral adrenal region and good control of the adrenal vein (8,9). However, the main disadvantages are the complications associated with extensive incisions such as surgical site infection, incisional hernia and the need for bowel manipulation, increasing the risk of visceral injury, ileus and post-operative adhesions (8).

Against this background, LA has been an attractive option for both patient and surgeon with its reduced invasiveness but without compromise of the ability to visualise and resect the adrenal glands (9). In our study, there were two patients that required a conversion from LA to OA, and its indications were similar to other studies including dense adhesions, bleeding uncontrolled by LA with impaired visualisation and a large lesion suspicious for gross malignancy (11).

In retrospective studies, LA has been shown to have a number of demonstrable benefits over OA, including decreased morbidity, less postoperative pain, less blood loss and shorter length of hospital stay (12). Additionally, it is believed that it allows improved visualisation and faster access to the adrenal vein, reducing the risk of catecholamine release (13). Our study has confirmed the findings of others that patients undergoing LA require a stay in hospital for significantly shorter periods of time postoperative and reduced blood loss (3-9). LA is also associated with fewer postoperative complications than OA. In a prospective case-controlled study comparing LA and conventional open posterior adrenalectomy, Thompson and colleagues demonstrated that early and late morbidity were significantly decreased in the LA group (14). Also, Gagner and colleagues noted that the main advantages of LA were the reduced rate of respiratory complications and the dramatic decrease in wound complications (15). In our series, the main complications from LA were bleeding, infections and injuries to surrounding organs such as large intestine and spleen. OA had the complications associated with LA, as well as additional pulmonary complications such as pneumothorax during dissection of the right triangular ligament of the liver, which is consistent with the literature. We recognise that in this study caution is required in interpretation of increased blood loss, longer operation times and increased morbidity in OA as the tumour sizes in the OA was on average larger, which could have contributed to the data. A beneficial future study would be to control for the size of the tumour while investigating differences between LA and OA.

Regarding operating times, many groups have reported longer procedure times when performing OA versus LA (16-17). Mellon and Sundaram noted that the average operative time for LA pheochromocytomas was 181.4 minutes compared with 174.8 minutes with OA, and MacGillivray’s group also noted that the mean operative time was significantly longer for LA than for OA (289 vs 201 min; p=0.042) (13,18). Hartmann et al. showed that using data of 171 LA procedures, the average operative time was 62 minutes (38-200mins) (19). It is likely that the prolonged operation times for LA when compared to those who had OA in our study are in keeping with the experience of others and undoubtedly
reflects, to some degree, the learning curve for this technically demanding procedure. As the knowledge and experience with LA continues to grow, we expect the trend in operation times to reduce even further in the future.

One of the benefits of LA is a significant decrease in mean hospital stay, and it was hoped that total hospital costs would also decline. Our study showed that the mean bed stay cost was significantly less in LA than OA, owing to a significantly earlier discharge: lower general ward costs (nurses, laundry, consultation by doctors), critical care costs, pharmaceuticals, pathology, imaging and allied health. The mean operation cost, which consisted of labour and non labour costs, were comparable between LA and OA, and it may be explained by a reduction in mean operation time but higher complication rate and blood loss in the OA compared to significantly smaller blood loss and complications, albeit higher labour and non labour costs owing to technically demanding procedure and instrumentation. The higher cost of instrumentation in LA was also found by Jacobs et al. who also reported higher cost of central supply of materials related to LA (7). The costing in this study was based on average costs rather than computing exact costs, and it would be beneficial for a future study to provide more precise comparison of costs between LA and OA. Also, this study did not investigate whether the cost of consumables could vary between 1980-2010, perhaps due to reusage of equipment in the earlier years compared to single use items in the 21st century. Finally, we acknowledge that the long time frame of this study has limitations regarding post-operative costs. It is likely that there has been a change in attitude to post-operative care between 1980-2010 with increased awareness of the advantages in mobilising patients early post-operatively and earlier discharge with community based care such as nursing and wound care. It would be an advantage to investigate and include these factors in the costing. Despite this, our study strongly suggests that there was saving in the mean total cost in the LA compared to OA. As we continue to become more proficient in LA procedures, a greater cost saving is envisaged in the future.

The results of the present study confirmed that LA is a safe, appropriate and cost effective surgical technique which compares favourably to those who had OA. It justifies this approach as an appropriate and viable method for patients requiring adrenalectomy where it is an option.

**Acknowledgements:** The authors would like to acknowledge the contributions of Dr Connor O’Meara for professional advice and support. This project was completed with intramural support from the Australian National University Medical School and Australian Capital Territory Health.

**Conflicts of interest:** Nil

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### Table 3. Perioperative and postoperative parameters for LA and OA. N.S= Statistically not significant.

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic (n=27)</th>
<th>Open (n=61)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Perioperative (mean ±SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean operating time (mins)</td>
<td>167.96 ±60.3</td>
<td>153.4 ±68.45</td>
<td>N.S</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>231.13 ± 242.9</td>
<td>542.43 ± 658.1</td>
<td>0.038</td>
</tr>
<tr>
<td><strong>Postoperative (mean ±SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complications (no.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>0</td>
<td>3 (4.9%)</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>1 (3.7%)</td>
<td>2 (3.2%)</td>
<td>-</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>1 (3.7%)</td>
<td>2 (3.2%)</td>
<td></td>
</tr>
<tr>
<td>Complicated Hematoma</td>
<td>1 (3.7%)</td>
<td>3 (4.9%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3 (11%)</td>
<td>10 (16%)</td>
<td></td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>5.46 ±3.8</td>
<td>9.86 ± 3.89</td>
<td>0.000004</td>
</tr>
</tbody>
</table>

---

**Figure 3.** A. Mean operation cost for OA and LA B. Mean bed stay cost for OA and LA C. Mean total cost for OA and LA. This was derived by adding the mean costs of operation cost and bed stay costs. Error bars indicate SD * p=0.00007, **p=0.02
REFERENCES

Barriers and solutions to the implementation of diabetes management plans in a rural Aboriginal health service

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*The University of Melbourne

INTRODUCTION

An Aboriginal Medical Service (AMS) asked for an assessment of their diabetes management procedures in order to improve practice. A recent turnover of staff had helped identify various deficits between practised and ideal management, and in measured outcomes. This was particularly evident with regards to diabetes, one of the national health priorities. As a disease rooted in lifestyle risk factors with a chronic course, the success of diabetes care provides a measure of the broader functioning and community integration of health practice. Access, cultural safety, interprofessional team practice and innovative models of health delivery underpin outcomes.

The AMS employs two general practitioners (GPs), two practice nurses, a health promotion officer, and Aboriginal Health Workers (AHWs). It is government-funded and meets stringent reporting requirements.

A hospital is located close by the AMS and emergency transfer to a tertiary facility is provided by ambulance. Specialist and allied health access is available within most areas, as shown in Table 1.

BACKGROUND

Diabetes

The Aboriginal population suffer the highest prevalence of diabetes in Australia with Aboriginal people self-reporting diabetes 10-20 years younger than non-Aboriginal Australians, and some of the highest complication rates in the world (1-3). In the National Health Survey conducted by ABS in 2001, at ages 35-44 years and 45-54 years about 10% and 20% of Aboriginal persons reported diabetes respectively, while among non-Aboriginal persons there were about 2% and 3% reporting diabetes at the same ages (7). In other studies Type 2 diabetes mellitus (T2DM) has been reported in 25% to 60% of Aboriginal community populations, with the risk of an Aboriginal person having diabetes 5-10 fold the Australian risk (4-6). These estimates are well above the Australian Bureau of Statistics (ABS) data (7), which while likely to be an underestimate (8), are in themselves cause for concern.

Modifiable risk factors including diet, exercise, waist girth and smoking (9-11) require culturally-appropriate educational interventions placed within a Medicare or otherwise public-funded avenue in order to be accessible to all Australian Aboriginal diabetic patients. The management of diabetes involves prevention or delay of complications, as well as detection and treatment of complications as they arise, thus necessitating a multi-disciplinary team approach to life-long patient care. The ideal management process aimed for by the AMS is shown in Figure 1.

Interventions aim to control blood sugar, hypertension, lipid profile and cholesterol, all of which contribute to the risk of cardiovascular disease in patients with diabetes (12,13). A scheme for clinical
management of diabetes is shown in Figure 2. Blood sugar has proven particularly difficult to control in Australian Aboriginal patients, as evidenced by persistently elevated HbA1c in several studies (11, 14), and should be prioritised in management to prevent micro- and macro-vascular complications.

Diabetes is a chronic, multi-system disease. Box 1 demonstrates the broad variety of complications that underpin the necessity of a team approach.

The importance of addressing and preventing each of these complications cannot be overemphasised, and given the considerable burden on the public health system, programs that do so are likely to be highly cost-effective (21, 22).

Access to healthcare
Access to healthcare is an often-cited issue in rural health (23, 24). This broad term was divided into five dimensions or themes (31,32) namely:
1. Availability (adequacy of supply of requisite resources)
2. Accessibility (location and transport availability)
3. Accommodation (logistics and organisation of service)
4. Affordability (cost of healthcare in relation to client’s means)
5. Acceptability (attitudes and comfort with the service).

Barriers to diabetes care in rural Aboriginal health settings have been previously cited as lack of resources, information technology, absenteeism, staff discontinuity, burden of treatment (cost), patient acceptability of services, lack of work-practice support and competing demands of acute care (21, 25).

Lack of work-practice support and competing demands of acute care underpin barriers in retaining staff. Patient acceptability of the health services is an element that overlaps with the concept of cultural safety.

Cultural Safety
Aboriginal people have long-suffered reduced access to mainstream health services because of perceived racial prejudices and cultural differences (26). The inclusion of AHWs has been shown to be associated with better health outcomes in diabetes care (27-29). In the Northern Territory, it was found that the ratio of AHWs to residents in the community was correlated to delivery of guideline-scheduled diabetes services (27). Improved healthcare delivery through AHWs makes their inclusion enormously cost-effective; “every year of dialysis deferred for one patient could fund the appointment of two health workers” (29). The utilisation of adequately supported AHWs with ongoing training and clearly defined roles provides immense measurable benefit and should be incorporated into diabetes healthcare plans.

Table 1. Services available for diabetic patients.

<table>
<thead>
<tr>
<th>Resident Specialists</th>
<th>Visiting Specialists</th>
<th>Allied health</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Practitioners</td>
<td>Cardiologists</td>
<td>Physiotherapist</td>
</tr>
<tr>
<td>Anaesthetists</td>
<td>Dermatologists</td>
<td>OT</td>
</tr>
<tr>
<td>Dental</td>
<td>Neurologists</td>
<td>Dietician</td>
</tr>
<tr>
<td>Emergency physicians</td>
<td>Orthotists</td>
<td>Diabetes educators</td>
</tr>
<tr>
<td>General Physicians</td>
<td>Renal Physician</td>
<td>Social work</td>
</tr>
<tr>
<td>General Surgeons</td>
<td>Vascular Surgeon</td>
<td></td>
</tr>
<tr>
<td>Ophthalmologists</td>
<td>Haematologist</td>
<td></td>
</tr>
<tr>
<td>Orthopaedic surgeons</td>
<td>Rheumatologist</td>
<td></td>
</tr>
<tr>
<td>Radiologists</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urologists</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Services occasionally required by diabetic patients

| Ear, Nose and Throat | Geneticists | Incontinence therapy |
| Obstetrics and Gynaecology | Cosmetic Medicine | Speech therapy |
| Paediatricians | Oncologist | |
| Psychiatrists | Radiation Oncologist | |
| Respiratory Physicians | | |
| Sports Medicine | | |

Aboriginal patient arrives at the AMS

Welcomed by AHW, explains processes

Follow-up monitoring e.g. BP, glucose

GP for consult and review

Medical referrals

Nurse for coordination and referral

Allied health referrals

GPMP & TCA

Weekly case reviews

Figure 1. Ideal management process at the AMS.
**Interprofessional team practice**

Team practice, integral to rural practice (24), is perhaps even more essential in managing chronic illnesses in the Aboriginal population. The challenges of competing demands of acute care cited earlier can be divided amongst an integrated team, and the barriers of effective communication to diabetes healthcare mediated by an AHW. Screening and monitoring of a widely dispersed and mobile population may also effectively be conducted by AHWs (30). By incorporating a focus on prevention and treatment with more continuity of care, healthcare teams are better placed to meet community needs (8, 31).

Multidisciplinary approaches are indisputably advantageous when they work well (24, 31). They rely on adequate staffing, good communication, clear role definition and workplace support and training (27), and thus require specific models of health service delivery.

**Health Service Delivery**

Health service delivery describes the coordination of personnel and resources. Models differ in urban and rural settings, and an Aboriginal Medical Service (AMS) is a model of practice incorporating GPs, nurses and AHWs to meet community needs (32).

The efficiency and effective delivery of these models correlates to health outcomes, as has been demonstrated by research into AMSs in the Northern Territory (20). Health markers including HbA1c levels were improved in association with three measures:

1. **Level of organisational influence** (including goals for chronic care, improvement strategies and incentives for care)
2. **Delivery system design** (planning and coordinated actions of multiple caregivers)
3. **Clinical information systems** (computer registry, an important element of which is the ability to provide treatment planning reports as well as the visit record)

These reflect the presence and utilisation of incentives within diabetes care plans, awareness of therapeutic guidelines and their facilitation by computerised systems and prompts. Medicare incentives have been revamped to utilise team practice, with the introduction of the general practice management plan (GPMP) and team care arrangements (TCA). Information systems that are user-friendly and regularly updated facilitate effective ongoing management, communication between caregivers and cohesive team practice.

**METHODS**

We sought to analyse current practice at the AMS to formulate avenues for the improvement of diabetes care. The results and analysis of these practices were presented to the clinic and provided the basis for recommendations of avenues for improved, coordinated diabetes care.
Box 1. Key features of a diabetes consultation. Adapted from Si D, Bailie R et al 2005 (20) with examples of studies concerning increased prevalence of complications as shown.

<table>
<thead>
<tr>
<th>Basic measurement</th>
<th>Risk factors; Physical measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td></td>
</tr>
<tr>
<td>BP</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Eye check</th>
<th>Ophthalmic complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual Acuity</td>
<td></td>
</tr>
<tr>
<td>Cataracts</td>
<td></td>
</tr>
<tr>
<td>Fundi (dilated pupils)</td>
<td></td>
</tr>
<tr>
<td>Ophthalmologist review</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Feet check</th>
<th>Podiatric complications (16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Check done</td>
<td></td>
</tr>
<tr>
<td>Sensation Peripheral pulses</td>
<td></td>
</tr>
<tr>
<td>Pressure areas</td>
<td></td>
</tr>
<tr>
<td>Infections</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Laboratory investigations</th>
<th>Risk factors; Diabetes control</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSL</td>
<td></td>
</tr>
<tr>
<td>HbA1c</td>
<td></td>
</tr>
<tr>
<td>Fasting lipids</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td></td>
</tr>
<tr>
<td>Urine- Dipstick</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
</tr>
<tr>
<td>ACR</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Counselling/Advice</th>
<th>Risk factors; Lifestyle and preventative measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td></td>
</tr>
<tr>
<td>Activity</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
</tr>
<tr>
<td>Diabetes medications</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immunisations</th>
<th>Infections (19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu vac.</td>
<td></td>
</tr>
<tr>
<td>Pneumo vac.</td>
<td></td>
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</tbody>
</table>

A telephone poll of 32 out of a total of 107 Aboriginal patients with T2DM was conducted with the aim of evaluating access, barriers and preferences in diabetes education. Questions asked are shown in Box 3.

Of the 75 who did not respond, one person was unable to answer questions as they were at work, 28 patients were not contactable as their phone numbers were incorrect or out-of-date, and 46 were unavailable as the patient was not at home to answer the phone. 100% of those available to talk participated in the survey, indicative of the community acceptance of the AMS.

It was suggested by the AHWs that the large number of patients who could not be contacted reflects the mobile nature of the population. The AMS regularly updates contact phone numbers. It would further be beneficial to link all AMS contact details across the state, or nationally.

RESULTS AND DISCUSSION

The themes emerging from the interviews with staff and patients are discussed below. The main themes related to access, cultural safety, interprofessional team practice, and health service delivery. Recommendations are also discussed.

Access

Access was examined by breaking it into the five dimensions described previously. Availability is addressed by the very existence of the AMS and proximity to neighbouring hospital, dental clinic and mental health service. Staff discontinuity was a problem at the AMS, in particular with high turnover of AHWs, and one of the recommendations made was to increase the recognition and support of staff. Accessibility is facilitated by free transport for Aboriginal clients. Accommodation may be limited by the absence of a flexible walk-in clinic. Acceptability is also well-addressed by the fact that it is an AMS. Affordability should not form a barrier as
all costs are covered by the government-funded clinic.

In general, the access at the AMS was very good, but could be improved upon by addressing the underlying reasons for staff turnover, and adding the flexibility of walk-in clinic sessions.

Cultural Safety
The AMS is a community-run, culturally safe service which employs AHWs and where the principles of cultural safety are enacted at all levels. However there are concerns that patients may be getting lost when referred to the nearby, more mainstream hospital services. Observations on cultural safety are described in Table 2.

Interprofessional Team Practice
The functioning of the team governs the chronic management of patients with diabetes.

Some practices have utilised AHWs as the central liaison between patients and the doctors or nurses. Whilst not the case at this AMS, AHWs were better supported than in the past and outcomes of visits were increasingly communicated and acted upon. Deficits in communication were evident on speaking to the practice nurses, who did not automatically see every diabetic patient and, in some cases, were not aware that a patient had diabetes. Although situated close by, the hospital had little interaction with the AMS and the Aboriginal health liaison officer had no existing links with the AMS.

As part of the evaluation and suggestions put to the AMS, it was recommended that weekly to fortnightly case conferences involving AHW, nurses and GPs could improve this interaction and team practice. It was suggested that each diabetic patient should see a practice nurse as well as the doctor to ensure all appropriate referrals were made. Links with the hospital should also be established.

Health Service Delivery
Chronic disease management necessitates organised records, education and detailed management plans. At the AMS, two central issues to service delivery were information systems and the utilisation of appropriate Medicare items in line with the national health priorities.

Communicare is an information system utilised by many Aboriginal Medical Services. Staff interviewees felt that as a system, it contained all the necessary components, but was difficult to use. This element within models of health delivery has been correlated to health outcomes (20), and should be addressed at the AMS through updated systems and staff training. It would also be beneficial to patients if the various Aboriginal Medical Services were linked to transfer vital information about the transient populations.

Updated systems should reflect General Practice Management Plan (GPMP) and Team Care Arrangements (TCA) Medicare guidelines and item numbers, and facilitate their use. A summary of annual and monthly review items was presented to staff at the AMS. It is anticipated that their increased usage will facilitate effective case management, team involvement and coordination.

CONCLUSIONS
Diabetes is present in an overwhelming proportion of Australian Aboriginal people, for a multitude of reasons, many of which are modifiable. Despite identified barriers, the achievements by dedicated diabetes programs and medical services are remarkable and provide a platform to work up from.

From a review of the literature, semi-
structure interviews and a phone poll it was concluded that the AMS would benefit from:

• Improving access through closer networks
• Utilising AHWs as central liaising points
• Conducting regular case meetings that include the GPs
• Updating information systems to facilitate communication, management plans and Medicare item number usage

The project was time-limited and future research would be beneficial to explore the impact that changes to practice may have on patient glycaemic control and long term outcomes.

Results of the assessment were presented to the AMS, resources for continuing practice improvement were offered and interested parties were forwarded this report. It is anticipated that the findings will be useful in clinical practice or research, in particular for providing evidence in programme and clinic planning, facilitating team interaction and in constructing guidelines.

Acknowledgements: All of the staff at the AMS who remain unnamed for confidentiality, but were welcoming, informative and inspiring.

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Computed tomography utilisation in tertiary hospitals and community settings in the Australian Capital Territory and South Eastern New South Wales

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*Medical Student, The Australian National University

ABSTRACT

Objectives: Technological advances in Computed Tomography (CT) imaging have offered an accurate and efficient tool to clinicians for the diagnosis of many medical conditions. However, recent increased usage in both tertiary hospital and community settings has been questioned as inappropriate, as economic and physical burdens of this modality are being revealed. The study aims were to determine the use of CT scan use within a six year period in the Australian Capital Territory (ACT) and South Eastern New South Wales (SE NSW) and to identify the demographic distribution of utilisation.

Methods: This is a sample-based cross-sectional study using data collected from patient encounters in tertiary hospital and community settings, in the ACT and SE NSW, over a two week data collection period held each year in June-July from 2006-2011.

Results: Data were collected from a total of 8787 patient encounters with a CT utilisation rate of 5.8%. From 2006-2008 to 2009-2011, the utilisation of CT scanning statistically significantly increased from 4.8% to 7.2% (p = 0.001). The CT utilisation rate was significantly higher in the hospital than community setting (p=0.03). CT usage did not differ significantly between the 0-9 yr age group and older age groups.

Conclusion: An increase in the use of CT scan utilisation in the Canberra region over the time periods 2006-2008 and 2009-2011 was observed. Judicious use of CT needs to be guided by weighing the potential benefits of imaging against the risks of radiation exposure.

INTRODUCTION

Since its introduction in the 1970s, the demand and availability of computed tomography (CT) has increased, largely due to the relative ease, rapidity and accuracy of this imaging modality (1). However, there are increasing concerns with regards to the economic and health burdens associated with this diagnostic tool.

It is estimated that 14% of radiation to the population worldwide could be attributed to ionising medical imaging, with the attributable risk of tumour formation from ionising medical imaging in persons greater than 75 increasing from 0.6% to 1.8% in populations studied (2). Medical procedures have now become the main source of radiation exposure in individuals (3). This is seen in the Australian populace, where an estimated 65% of all medical radiation exposure is due to CT scans (4). This is of particular importance with the increase in the usage of diagnostic imaging modalities and their potential carcinogenic impact on patients, many of whom do not require such tests for diagnostic or therapeutic purposes (5).

The demand for CT investigations is dependent upon patient demographics, with an increased incidence of CT utilisation in older populations (6). This is likely related to the higher prevalence of disease in this group (1) and is significant due to an aging Australian populace. Additionally, with regards to younger populations, there is a fear of radiation-induced morbidity and mortality related to early tumorigenesis (7-9).

Due to the recent litigious culture, fear of legal prosecution influences physician judgement in selection of appropriate investigative tools (5) with defensive imaging accounting for as much as 19% of the total ordered investigations and 35% of total imaging expenditures (10). This is compounded by the public health funding system in Australia, provided by Medicare, which furthers the utilisation of imaging via consumer demand, the practice of defensive medicine and a lack of personal financial liability. Therefore, the potential benefit of CT investigation conferred to clinical decision making must be balanced against the potential for long term harm to patients as well as the health budget.

Primary aims of the study were to determine the use of CT scans during the study period 2006-2011 in the ACT and SE NSW, and to compare the use of CT scans between different demographic and health-care service populations.

METHODS

Patient data and consent were obtained by consecutive year 3 medical student cohorts at the ANU over the period of May-June in the years 2006-2011. Study approval was granted by The ANU Human Research...
Data were collected from defined locations including: The Canberra Hospital, Calvary Hospital, urban and rural general practices, and other community services. CT scans ordered in the hospital setting included those scans ordered in the emergency department, outpatient services and inpatient settings. Information was collected from health care encounters regarding patient demographics (age, sex, country of birth), the reason for health care encounter as well as reason, site, diagnosis, procedures carried out, investigations ordered, medicines prescribed and advice given. Data were entered into a database for analysis.

The inclusion criterion for the study was that a patient had a CT examination ordered during the health care encounter. Data were stratified according to age and encounter site. The paediatric group in this study was classified as those individuals aged 0-9 years, and the adults were classified as individuals belonging to the remaining age brackets (i.e. 10-19, 20-29... years). The encounter sites were ‘Hospital’ (The Canberra Hospital, Calvary Hospital), ‘Community’ which included general practice and community services, community health service, community paediatricians, ambulance, after hours medical centre, private rooms in the ACT and SE NSW and ‘Others’ which did not fit into either the ‘Hospital’ or ‘Community’ category.

Data were further divided into two main time periods (2006-2008 and 2009-2011) and for each time period the overall percentage of CT utilisation was calculated and compared. A comparison was also made of CT utilisation in the paediatric and adult groups in these time periods, as well as between the hospital, community and other health service settings.

Percentages were compared for statistical differences using the Chi square test, and an alpha level of 0.05 was used as the level of significance. Data analysis was performed using the statistical software package SPSS 19.0, SPSS Inc, USA.

RESULTS
A total of 8787 patients were reviewed for patient demographics and CT usage. The overall CT utilisation rate was 5.8%. The patient demographics are outlined in Table 1.

The mean age of all patients was 50.9 ± SD 25.4 years and 48.9% were male. The percentage of patients categorised as ‘Hospital’ was 50.6%, with 45.9% classified as ‘Community’ and 3.9% classified as ‘Others’. There was a statistically significant difference between the incidence of CT ordering in the ‘Hospital’ (6.4%) and ‘Community’ (5.2%) setting (p = 0.03). The incidence of CT ordering did not differ significantly between the ‘Hospital’ and ‘Others’ (5.9%) setting (p = 0.73). There was also no significant difference in CT ordering between the ‘Community’ setting and ‘Others’ (p = 0.62) (Table 2).

As a whole, the utilisation of CT scans increased from 2006 to 2011. (Figure 1 and Table 3). There was a statistically significant difference (p = 0.001) between the CT utilisation rate of 2006-2008 (4.8%) when compared to the 2009-2011 time period (7.2%).

The CT utilisation rate for the paediatric age group was compared with the rest of the population. There was no statistically significant difference (p = 0.11) in the CT ordering frequency between children aged 0-9 years (4.6%) when compared with those aged 9 years and above (6.0%). The frequency of paediatric CT utilisation in 2006-2008 was compared with that of 2009-2011, which showed no statistically significant difference between the two groups (p = 0.40).

DISCUSSION
The principal findings of this study were that there was an increase in utilisation of CT between 2006-2011 in all settings and there was a statistically significant difference in the ordering of CT scans between Hospital and Community settings.

<table>
<thead>
<tr>
<th>Setting</th>
<th>No. of Scans</th>
<th>No. of Patients</th>
<th>Percentage of patients with CT Scans (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital</td>
<td>282</td>
<td>4440</td>
<td>6.35</td>
</tr>
<tr>
<td>Community</td>
<td>200</td>
<td>3834</td>
<td>5.22</td>
</tr>
<tr>
<td>Others</td>
<td>30</td>
<td>513</td>
<td>5.85</td>
</tr>
<tr>
<td>Overall</td>
<td>512</td>
<td>8787</td>
<td>5.83</td>
</tr>
</tbody>
</table>

Table 2. Frequency of CT scans ordered by clinical setting
While the use of CT scans was higher in adults than children, this was not a statistically significant difference.

Our study demonstrated that in the ACT and surrounding SE NSW, the CT utilisation rate significantly increased from 4.8% in 2006-2008 to 7.2% in 2009-2011 (p < 0.05). This finding is consistent with the literature (2) which has also shown increases in CT utilisation over a larger time frame. Possible reasons for this rate of increase include fear of litigation, poor communication between physicians and a fall in physician confidence (5, 10). Our results also demonstrated that overall CT usage was significantly higher in the Hospital than Community settings (p<0.05). Although we did not collect data on the distribution of CT scanners throughout the ACT and surrounding SE NSW, this finding probably reflects the higher availability of CT scanners at hospitals. The proportion of patients with severe or life-threatening disease is likely to be higher in the hospital setting, thus resulting in more frequent utilisation of CT. However, the greatest increase over time was in the community setting and this actually exceeded hospital usage in 2011.

In terms of age distribution, the use of CT scans is higher in older age groups although it was not a statistically significant difference in our data. This is likely related to the higher prevalence of disease states as a person ages (1).There has been increased use of CT examinations in children under 15 years of age in developed countries (11), however, in recent years, there has been an increased awareness of the risk of long-term malignancies such as leukaemia following exposure to ionising radiation in childhood (9). Accordingly, many hospitals are minimising CT-associated radiation risk by ensuring that any paediatric CT examination is justified, and by considering alternative modalities such as ultrasound and magnetic resonance imaging (11). Our data showed a CT utilisation rate of 4.6% for ages 0-9 years and 6.0 % for ages 10 years and up. It is likely that this was not statistically significant because of the small paediatric sample size. The low utilisation rates may reflect more rigorous indications for paediatric CT examinations in the ACT and SE NSW.

There are some limitations to this study. The data were all collected in the middle of the year and were collated by students on any consecutive days within a three week time period. This may have led to a selection bias. Improving randomisation of participant selection may help improve this. There was a lack of information in the database regarding type and indication for CT and so it was not possible to examine the different contexts in which such decisions were made. Future changes to the data collection would allow such exploration.

In conclusion, our study suggests that there is an increase in the utilisation of CT scan in the ACT and SE NSW between 2006-2011. Judicious consideration of the diagnostic benefits and convenience of CT scanning needs to be weighed against the long term risks of radiation.

Conflict of interest: None
Acknowledgements: Dr Ashwin Swaminathan provided valuable guidance as supervisor.

Table 3. Percentage of patients with CT scan ordered by year

<table>
<thead>
<tr>
<th></th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2006</td>
</tr>
<tr>
<td>Hospital</td>
<td>7.19</td>
</tr>
<tr>
<td>Community</td>
<td>4.49</td>
</tr>
<tr>
<td>Others</td>
<td>7.27</td>
</tr>
<tr>
<td>Overall</td>
<td>5.99</td>
</tr>
</tbody>
</table>

Figure 1. Percentage of patients with CT scans ordered by year

[Table and Figure]
REFERENCES


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INTRODUCTION

Inappropriate pathology testing creates unnecessary patient discomfort, consumes limited hospital resources and negatively impacts on medical staff efficiency. High rates of unnecessary pathology test ordering have been documented in international studies (1-5). Miyakis et al (6) reported 68% of laboratory tests ordered in a Greek internal medicine department did not contribute towards the management of patients. Furthermore, a Canadian population based study (2) found repeat testing of eight commonly ordered pathology blood tests within three months accounted for 40% of overall test utilisation and estimated that up to $36 million Canadian dollars was spent annually on test repetition nationwide. Additionally, Kwok and Jones (7) found repeat requests made up 17% of total laboratory workload and estimated annual costs of redundant immunology tests to total US $132,151 for their unit. Interventions have been designed to reduce such ordering patterns however the optimal form of intervention is unclear (8,9).

Although a number of studies have demonstrated significant levels of inappropriate pathology test ordering, all have used various classifications, methods and clinical settings (5-11). This wide variability across studies is reflected in reported inappropriate test or utilisation rates ranging anywhere between 4.5% and 95% (4).

This study aimed to determine the level of inappropriate blood test ordering in a tertiary-level Australian hospital setting and whether a low-cost educational intervention could reduce the level of inappropriate ordering.

ABSTRACT

Aims: Inappropriate ordering of pathology blood tests consumes limited healthcare resources. We aimed to assess the incidence of inappropriate pathology ordering by medical units in a tertiary level Australian hospital, and to determine whether a multi-faceted educational intervention can reduce the rate of inappropriate ordering.

Methods: A baseline retrospective audit was conducted of the ordering frequency of 14 common ('sentinel') blood tests at an Australian tertiary level hospital. The initial audit comprised 360 randomly selected medical unit in-patients admitted over a 12-month period (December 2008 - November 2009). A multi-faceted education campaign for junior hospital doctors followed (June 2010). Further audits of sentinel blood test ordering occurred for 150 randomly selected in-patients at one month (August 2010), and six months (January 2011) post-intervention. The appropriate ordering frequency for sentinel blood tests was defined according to conservative criteria developed after review of relevant scientific literature, clinical guidelines and expert opinion.

Results: Of the 4805 sentinel tests audited pre-intervention, 218 (4.5%) were inappropriate by study criteria. The post-intervention audits revealed inappropriate ordering had reduced to 1.5% (p <0.0001) at 1 month and 2.9% (p< 0.0001) at 6 months relative to baseline.

Conclusions: A multi-faceted intervention reduces inappropriate ordering with benefits for patients, staff and hospital finances. Ongoing education strategies are required to maintain this benefit.

METHODS

Study Setting

The Appropriate Pathology Test Study (APTS) was conducted at The Canberra Hospital (TCH), a 600-bed tertiary level teaching hospital situated in the Australian Capital Territory (ACT), Australia.

Study Phases

The study was carried out in three phases: Pre-intervention, Intervention and Post Intervention.

Pre-Intervention

A retrospective, baseline audit of blood test ordering for 360 medical in-patients admitted between December 2008 and November 2009 inclusive, was conducted. These patients were selected randomly from the electronic medical records database, and were eligible for selection if above the age of 18 years and admitted to a medical unit for more than 24 hours. To ensure an even representation across medical units (and allow comparison between units), patient records were derived from three medical unit groupings of 120 patients each: (1) Aged Care, (2) General Medicine (72-hour short stay unit) and (3) Composite medical units

Although a number of studies have demonstrated significant levels of inappropriate pathology test ordering, all have used various classifications, methods and clinical settings (5-11). This wide variability across studies is reflected in reported inappropriate test or utilisation rates ranging anywhere between 4.5% and 95% (4).
(including gastroenterology, cardiology, renal medicine, oncology, dermatology, endocrinology, haematology, immunology, infectious diseases, neurology, and rheumatology). Ten records were chosen at random for each month per medical unit grouping to allow for seasonal differences in ordering.

Test selection and analysis
Pathology blood test ordering for each admission was accessed using the hospital electronic pathology information system. As well as recording the overall number of pathology blood tests ordered per admission, 14 common pathology blood tests were used as ‘sentinel’ markers to assess the appropriateness of the frequency of ordering (Table 1). These tests were chosen because they are commonly ordered in a hospital setting and are therefore likely to reflect the overall rate of inappropriate ordering. Through review of current guidelines and discussions with senior clinicians, conservative criteria were developed by which inappropriate ordering frequency of sentinel tests could be defined – essentially where re-ordering of a test within a certain timeframe was illogical (based on biological or biochemical grounds) or very unlikely to lead to a change of management. A test was defined as being inappropriately ordered if the test was re-ordered more frequently than that defined by these criteria.

Intervention
Following the initial audit, a multifaceted intervention was conducted involving surveys, an education session for junior doctors, placement of study posters in doctors’ work areas throughout the hospital, and distribution of laminated information cards (lanyard) to doctors to be worn with their hospital ID badge. The surveys assessed what factors influenced pathology test ordering and 55 medical unit doctors (7 interns, 11 residents, 24 registrars & 13 consultants) from TCH completed an anonymous questionnaire. The questions addressed the doctor’s knowledge and opinions on test costs, awareness of appropriate test intervals and how to improve the ordering process. The posters and information cards publicised the findings from the initial audit regarding rates of inappropriate pathology test ordering, costs of individual tests and advice promoting sensible pathology ordering practice.

Post-Intervention
Follow-up audits (using the same protocol as the pre-intervention audit) for 150 in-patients was conducted at one-month (August 2010) and six months (January 2011) post-intervention.

Ethics Approval
Approval was gained to conduct this study from the Human Research Ethics Committees of The Australian National University and Australian Capital Territory Health.

Statistical analysis
The length of admission (days), number and type of all pathology blood tests ordered during admission were recorded for each patient. The percentage of inappropriate requests was calculated for each sentinel test (number of inappropriate sentinel tests / total number of sentinel tests ordered x 100). A crude measure of financial burden of inappropriate ordering for sentinel tests was determined by the following equation:

\[(\text{Cost of sentinel test (based on the Australian Medicare Benefit Schedule)} \times \text{Average rate of inappropriate sentinel test ordering per admission}) \times \text{(Number of admissions to medical units per year)}\]

RESULTS
The characteristics of the patient populations randomly selected for pre- and post- intervention audits are shown in Table 2. Although the audit populations were

<table>
<thead>
<tr>
<th>Sentinel Pathology Test</th>
<th>Abbreviation</th>
<th>Inappropriate testing if repeat ordering occurred within:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-nuclear Antibody</td>
<td>ANA(6)</td>
<td>28 days</td>
</tr>
<tr>
<td>C-Reactive protein</td>
<td>CRP(12)</td>
<td>1 calendar day **</td>
</tr>
<tr>
<td>Electrolytes, Urea and Creatinine</td>
<td>EUC(3)</td>
<td>1 calendar day **</td>
</tr>
<tr>
<td>Erythrocyte Sedimentation Rate</td>
<td>ESR(12)</td>
<td>1 calendar day **</td>
</tr>
<tr>
<td>Iron Studies</td>
<td>Fe studies(1,2)</td>
<td>8 weeks</td>
</tr>
<tr>
<td>Folate</td>
<td>Folate*</td>
<td>90 days **</td>
</tr>
<tr>
<td>Glycosylated Haemoglobin</td>
<td>HbA1C(1,2)</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Liver Function Tests</td>
<td>LFT*</td>
<td>1 calendar day **</td>
</tr>
<tr>
<td>International Normalised Ratio</td>
<td>INR(13)</td>
<td>1 calendar day **</td>
</tr>
<tr>
<td>Prostatic Serum Antigen</td>
<td>PSA(14,15)</td>
<td>6 months</td>
</tr>
<tr>
<td>Parathyroid Hormone</td>
<td>PTH*</td>
<td>28 days</td>
</tr>
<tr>
<td>Thyroid Stimulating Hormone</td>
<td>TSH(16)</td>
<td>28 days</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>Vit B12(1)*</td>
<td>90 days **</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Vit D(17)*</td>
<td>8 weeks **</td>
</tr>
</tbody>
</table>

*These repeat intervals were determined by consulting expert opinion
**If first test result was within reference limits for test.
*** If previous test was outside of reference limits

Table 1. ‘Sentinel’ pathology blood tests and appropriate testing interval
The pre-intervention audit showed a total of 9046 blood tests ordered for all 360 patients equating to an average of 25 tests per admission. The total number of blood tests ordered for each admission at six months post-intervention had not significantly changed relative to either the pre-intervention or one month post-intervention figures. From the initial audit, the total of sentinel blood tests (4805) accounted for 53% of tests ordered overall and according to our study criteria, 4.5% (218) of sentinel blood tests were inappropriately ordered. In the one-month post-intervention audit there was no significant change in the number of total blood tests ordered for each admission (25 tests per each admission). However our data show a significant reduction in the proportion of inappropriately ordered sentinel tests to 1.5% (29 tests, p<0.0001). At six months post-intervention this proportion of inappropriately ordered sentinel tests remained lower than our initial pre-intervention result, however it had increased relative to that at one month post-intervention. Table 2 shows that at baseline there were 218/4805 (4.5%) of sentinel tests that were inappropriately; at one-month post-intervention there were 29/1928 (1.5%) which was statistically significantly different from baseline (p<0.0001) and at six months post-intervention there were 52/1822 (2.9%) also statistically significantly different from baseline (p<0.0001).

Sentinel tests with long minimum time interval between testing had the highest proportion of inappropriate ordering, although ordered relatively infrequently. Sentinel tests with shorter minimum time intervals were inappropriately ordered at a lower rate, however because of their high frequency of ordering overall, the total number of these inappropriate tests was high. In particular, CRP – a nonspecific marker of inflammation – was ordered once every two and a half days on every patient and therefore was included in the more prominent category of inappropriate tests. However these trends become less prominent at six-month post-intervention, suggesting that the effect of the intervention wanes with time.

DISCUSSION

To our knowledge, the Appropriate Pathology Test Study (APTS) is the first attempt to determine the prevalence...
of inappropriate pathology blood test ordering in an Australian hospital. Our pre-intervention audit revealed an inappropriate blood test ordering proportion of 4.5% translating to a significant financial burden for the hospital. In addition, we found that certain tests (i.e C-reactive protein, EUC and LFTs) are ordered very frequently and even though not meeting our criteria for inappropriate ordering, are likely not to be consistent with good clinical practice (figure 1). We have shown that a multi-faceted and cost effective intervention can significantly reduce the rates of inappropriate test ordering.

Previous studies have reported large variations in prevalence of inappropriate pathology testing ranging from between 4.5–95%(4). This variation is attributable to different criteria used to determine test appropriateness, resources employed and clinical setting. For example, Miyakis et al (7) reported an inappropriate pathology test rate of 68%, based on a case-by-case review of patient clinical data (e.g history, examination, investigations, and outcomes). Their method was comprehensive, however classification of test appropriateness was necessarily subjective. The strength of our study is that we used conservative criteria and simple reproducible auditing measures.

A meta-analysis (11) comparing the effects of different interventional strategies found that successful interventions should be directed at multiple behaviours, be cost effective, sustainable, and customised for the particular hospital setting and staff. Our intervention met these criteria and formed the basis for an ongoing education strategy. The one-month post-intervention audit showed our intervention to be successful in the short term with inappropriate test proportions decreasing to 1.5% (p<0.0001), a 67% improvement from baseline.

A Computerized Physician Ordering Entry (CPOE) system has been advocated in numerous studies(10). This would have the advantages of improving staff efficiency, hospital expenditure and quality of patient care. However, the introduction and maintenance of such systems is often cost prohibitive for many health care providers. We were able to show in our study, that a cost effective educational system was able to provide a significant reduction in inappropriate pathology testing. Enhancement and expansion of such a program throughout a hospital may obviate the immediate need for introduction of a CPOE.

Survey and audience responses from our educational session provided good insight into why pathology tests (appropriate or not) are ordered. The major factors influencing pathology test ordering was intuitive, however the discrepancy of responses between junior and senior doctors in terms of cost and patient comfort was noteworthy. This result suggests that targeting junior doctors may be preferable in future planned interventions, an important population given that they order the majority of blood tests in a hospital setting.

We did note a waning effect of our intervention over time, which was consistent with other studies(18,19). It would be important to reinforce the key messages of the intervention at various time points throughout the year. Furthermore, this would help change the mind-set of physicians to give careful consideration of pathology testing which enhances the delivery of clinical medicine and the physician experience.

Our study has some limitations. Firstly, this was a single centre study and may not be able to be generalised to other health facilities. Secondly, because one and six- month post-intervention audits only measured pathology blood tests ordered within a one month period, seasonal effects of ordering due to staff changes and disease variation throughout a year may not have been accounted for; nevertheless, comparing August of 2009 and 2010 reveals a significant improvement of 64% (p <0.0001). Despite these shortcomings, our study was important in providing evidence of inappropriate pathology blood test ordering in an Australian hospital setting and the effect of a simple, cost-effective and multifaceted intervention on pathology blood ordering.

CONCLUSION

Inappropriate blood test ordering leads to increasing financial costs and patient morbidity(6,7). We have shown a simple, multi-faceted and cost-effective intervention was successful in reducing the rates of inappropriate pathology test ordering.

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The impact of maternal employment on infant attachment and cognitive development
A Literature Review

Erin O’Reilly Bsc(Psych)(Hons)*
*Medical Student, The Australian National University

INTRODUCTION

Over the past thirty years it has become increasingly common for mothers to return to paid employment within a year of their infant’s birth (1). The implications of this change for infant social, emotional and cognitive development has generated widespread interest within the field of psychology, as well as much debate and controversy (2). Although many researchers have found early maternal employment to have a negative impact on infant development, opposing research suggests that non-maternal care may in fact be beneficial to later child outcomes. This subject is of particular importance to health professionals, as rates of maternal employment continue to rise amid a climate of social change (3). This paper will provide a review of the literature to date on early maternal employment and its impact on infant development. Due to the scope of literature in this area, this review will primarily focus on maternal employment initiated within the first year of infancy and the effect of non-maternal care on infant attachment and cognitive development. This paper will begin by addressing the literature that has found early maternal employment to have a negative impact on these two important domains of infant development.

STUDIES SUGGESTING THAT EARLY MATERNAL EMPLOYMENT HAS A NEGATIVE IMPACT ON INFANT ATTACHMENT AND/OR COGNITIVE DEVELOPMENT

To study the potential effects of early maternal employment on the quality of infant-mother attachments, Barglow and colleagues recruited a small sample of mother-infant pairs from middle class, low risk families (4). Contrast groups were assigned according to maternal employment hours per week and infant-mother attachments were assessed using the Ainsworth Strange Situation (4). The results of this study suggest that early maternal employment significantly increases the likelihood of classifying an infant as insecurely attached. Infants of working mothers also scored higher on measures of avoidance compared to infants of unemployed mothers, rendering them more likely to be classified in the insecure-avoidant category (4). To explain the observed relationship between early maternal employment and the increased likelihood of insecure-avoidant attachments, Barglow and colleagues draw on Main and Weston’s explanation of avoidance behaviour in the Strange Situation. Main and Weston suggest that constant physical and psychological rejection by the mother makes an infant more susceptible to disorganised behaviours in situations of emotional distress (5). Therefore, avoidance of the mother allows

ABSTRACT

This paper reviews the topic as to whether early maternal employment has an impact on infant attachment and/or cognitive development. Current research has so far demonstrated opposing views in this area, making it difficult to ascertain whether early maternal employment is indeed more beneficial or detrimental to the developing infant. Evidence that has found early maternal employment to have a negative impact on infant development suggests that non-maternal care may have a detrimental effect on the quality of infant-parent attachments and later child cognitive outcomes. Opposing research suggests that no relationship exists between early maternal employment and the quality of infant-parent attachments, and that non-maternal care may be beneficial to infant cognitive development. Due to the conflicting views presented by existing research, it seems that further research is needed in this area to draw out more clearly the type and extent of the effect that early maternal employment has on the developing infant.

Interestingly, studies of father-infant attachment have also highlighted the potential effects of maternal employment on the quality of infant-parent attachments (6,7). In their aim to determine the effects of early maternal employment on the quality of infant-father attachments, Belsky and Rovine recruited a large sample of working and middle class families (6). Infants were observed in the Strange Situation with their fathers at age thirteen months and were placed in contrast groups according to the number of hours they spent in non-maternal care per week. The results of this study found that sons of mothers employed in excess of 35 hours per week were more likely to be insecurely attached to their fathers. In addition, sons of mothers employed in excess of 20 hours per week were more likely to be insecurely attached to both parents (6). To provide some insight into this observed relationship it is interesting to note that further research has found boys to be more vulnerable to less sensitive caregiving than girls
(8). Furthermore, boys are more commonly perceived by their parents to be less in need of sensitive care as infants compared to their female siblings (9). As caregiver sensitivity is a key predictor of secure infant-parent attachments this may provide some explanation for the prevalence of insecure father-infant attachments as observed by Belsky and Rovine (6). It is of further interest to note that fathers who are forced into providing infant care as a result of their wives employment are more likely to be insensitive in their care compared to fathers of unemployed wives (3). Therefore, maternal employment may increase unwanted family responsibility for fathers leading to frustration and resentment, which ultimately has an impact on father-infant relationships.

Although less research has been devoted to the effects of early maternal employment on infant cognitive outcomes, much of this literature has found early maternal employment to have a negative impact on child outcomes (1, 8). Using a large sample obtained from the National Longitudinal Survey of Youth, Baydar and Brooks-Gunn aimed to examine the relationship between early maternal employment and the cognitive outcomes of preschool aged children (8). In addressing the timing of maternal entry into the workplace, this study was further able to identify particular aspects of maternal employment that might be most harmful to infant development. In examining their results, Baydar and Brooks-Gunn found that in the first year of life maternal employment had a significant negative effect on cognitive outcomes for all children, regardless of gender or socio-economic status (8). Interestingly, these effects were most prevalent when maternal employment was initiated in the second and third quarters of the first year of infancy. In explaining these observations Baydar and Brooks-Gunn suggest that infants may be most vulnerable to maternal absence in the second and third quarter as they are only just beginning to form representations of their parents using newly developed cognitive concepts of object and person permanence (8). As these concepts are not properly formed in the first quarter and are more readily adapted in the final quarter, maternal entrance into the labour force during these periods may be less detrimental to the cognitive development of the infant (8).

In critique of the literature that has found early maternal employment to have a negative impact on infant development it is important to note that the Strange Situation has not been established as a valid measure of attachment security for infants of employed mothers (9,10). In particular, many researchers have suggested that the Strange Situation may not elicit an anxiety response in infants of employed mothers to the same extent as infants of non-employed mothers as they are inherently familiar with routine separation from their attachment figures (11). In this context, avoidance of the mother may not be indicative of insecure attachment relationships, but rather an appropriate response to a situation that is neither distressing nor unfamiliar (12). Furthermore, as independence is more valued by working mothers than their non-employed counterparts, infant avoidance behaviour may also be a response to parental expectations and training (12).

In critique of the literature on cognitive development in infants with working mothers, Baydar and Brooks-Gunn note that much of the past literature has been unable to control for important confounders (8). This problem is highlighted by studies that have come to conflicting conclusions regarding the effects of maternal employment despite using the same dataset obtained from the National Longitudinal Survey of Youth (1). The lack of appropriate control for confounders such as gender, race, birth order and family income are not restricted to studies of infant cognitive outcomes, but are also indicative of the literature concerned with the quality of infant-parent attachments (1, 9). Finally, as the majority of research in this field has not been longitudinally designed, it is unclear as to whether the effects of early maternal employment on infant cognitive development are long lasting or can be expected to dissipate over time (13).

STUDIES SUGGESTING THAT EARLY MATERNAL EMPLOYMENT HAS A POSITIVE, OR NEGLIGIBLE IMPACT, ON INFANT ATTACHMENT AND/OR COGNITIVE DEVELOPMENT

Using a relatively small sample of middle class, two-parent families, Chase-Lansdale and Owen aimed to examine the effects of early maternal employment on the quality of infant-mother attachments (7). Mothers were allocated to the employed category if they were employed for at least 38 hours per week and infant-mother attachments were investigated using the Ainsworth Strange Situation. Contrary to the results of Barglow and colleagues, no relationship was found between maternal employment status and the quality of infant mother attachments (4). In interpreting their results, Chase-Lansdale and Owen suggest that the theoretical underpinnings of the Strange Situation may have been widely misinterpreted by past researchers (7). In particular, they conceive attachment patterns to be more empirically related to the quality of care given by the mother, rather than the infant’s experience of the relative quantity of maternal presence and absence (7).

Using a large sample obtained from the National Longitudinal Survey of Youth, Harvey investigated the effects of early maternal employment on child cognitive development (13). Children of all races between the ages of 3 and 12 were included in the sample and were assessed using the Peabody Picture Vocabulary Test-Revised to provide a comparative measure of cognitive development. To control for confounders, controls were used for a wide array of background variables including family income, mother’s age, mother’s education and the child’s gender. Despite using the same data set as Baydar and Brooks-Gunn, the results of this study suggest that early maternal employment has only a small effect on child cognitive outcomes (8). A condition that may reduce the impact of early maternal employment on child cognitive development is provided by Zick and colleagues who have found that employed mothers are more likely to engage in reading activities with their children from infancy compared to non-employed mothers (14). In addition, employed mothers have also been found to be more highly interactive with their infants, particularly with respect to verbal stimulation (9, 15). This may be because employed mothers attempt to compensate for their lack of physical presence by spending the time that they do have with...
their children engaged in activities they perceive to be cognitively enriching (14). As rates of maternal employment are intrinsically linked to an influx of children into centre based care, it has been further suggested that the benefits of such care may have a positive impact upon infant cognitive development.

In research conducted by Clarke-Stewart, it was observed that the cognitive development of children placed in centre based care was considerably more advanced than children remaining in home care (16). To account for these findings Clarke-Stewart provides a major review of past research in which the most likely causes of the development differences of children in different care settings are considered (16). For the most part, Clarke-Stewart suggests that centre based care provides children with the opportunity to interact with a variety of different adults who are trained in child development (16). As care givers with professional training are more likely to be interactive and didactic in their caregiving, it is not surprising that children in their care make significant cognitive progress (16,17). Clarke-Stewart further suggests that the types of physical equipment provided in day care centres may present more of a cognitive challenge to children compared to those provided in the home (16). As teachers often direct children in more constructive play with materials than carers in the home setting, this may also be beneficial to a child’s cognitive development (16, 18). In the context of infant development, Clarke-Stewart further notes that children who have been in centre based care from infancy are more likely to show advances in their cognitive development compared to children entering day care at a later stage in life (16, 19).

In critique of the literature that has found no relationship between early maternal employment and the quality of infant-mother attachments, many of the same criticisms apply as mentioned in relation to the research finding early maternal employment to have a negative impact on infant-parent attachments. In regard to Chase-Lansdale and Owen’s study, it has been noted that mothers were recruited a year after the birth of their child, whilst in the study conducted by Barglow and colleagues, mothers were recruited during their pregnancy (4,7). Hence, in Chase-Lansdale and Owen’s study, an inherent confounder is likely to have operated in which mothers may have elected not to participate in the study if they knew their relationship with their infant was poor (7). By recruiting mothers prior to their infant’s birth, Barglow and colleagues may have avoided this inherent confounder by obtaining maternal allegiance to the study prior to the formation of infant-mother attachments (4).

On reflection of the literature which suggests centre based care may have a positive impact on later cognitive development, Belsky notes that much of this literature has failed to take into account important parameters of care such as the timing of separation from the mother and the quality of care received (2). Differences in child care environments, programs and settings are also important parameters of care that have been neglected by researchers in this field (16). Furthermore, it seems likely that infant personality, temperament and well-being may also mediate the impacts of centre based care on infant development. As mentioned earlier, literature concerned with the quality of infant-parent attachment and child cognitive outcomes has also been criticised for failing to adequately address potential confounders such as gender, parental income and the child-rearing attitudes of both parents (1,9).

CONCLUSION

In addressing the topic as to whether early maternal employment has a negative impact on infant development, this paper has found the existing literature in this field to be conflicting and not without limitations. Specifically, failure to control for important confounders within the literature on maternal employment makes it difficult to distinguish between valid studies and those that have been inadvertently biased in their findings (13). As this problem is symptomatic of the evidence that has led researchers to conclude that early maternal employment is both beneficial and detrimental to the developing infant, it seems that no clear conclusion can currently be made as to the type and extent of impact early maternal employment has on either infant attachment or cognitive outcomes.

In noting the discrepancies within the existing literature, Barglow and colleagues suggests that the effects of early maternal employment on infant development may be mediated by a number of factors that have not been easily identified by past research (4). Therefore, in future it may be more appropriate to consider early maternal employment as part of a larger system of family processes that together influence and mediate infant outcomes, rather than as an independent variable acting in isolation on child outcomes (3). By taking such an approach researchers may be able to identify the factors, that when combined with the impacts of early maternal employment, pose the most significant risk to infant social, emotional and cognitive outcomes (4). Although outside the scope of this paper, it is important to note that this review has not addressed many longer term issues beyond infant attachment and cognitive development that may have a positive and/or negative impact on later child outcomes. For example, there is evidence to suggest that mothers who are employed part-time are more likely in the long term to be involved in their children’s schooling, and that children of working mothers who are cared for by their grandparents are more likely to be overweight or obese (20,21). It is important to acknowledge the limited scope of this review as it is likely that child outcomes are dependent on a wide range of factors, occurring both in infancy and throughout the remainder of childhood, which may vary in terms of their presence and impact throughout the course of a child’s development.

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The molecular pathogenesis of primary erythromelalgia, a painful inherited syndrome – An update

A Literature Review

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CLINICAL MANIFESTATIONS

Erythromelalgia was first described by neurologist Dr Weir Mitchell in 1874 (1). Clinical manifestations include severe, burning and bilateral pain localised to the peripheries, especially the hands and feet, aggravated by warmth and exercise (2). Relief of pain occurs by immersing the extremities in cold, such as ice (3). The severity of this condition may progress to include a larger body area, and the pain may change from episodic to constant (3). The pain is associated with vasomotor changes in the peripheries (Figure 1), such as erythema and oedema (3). Erythromelalgia is considered primary if there is an absence of underlying causes such as myeloproliferative diseases (secondary erythromelalgia). In contrast to the primary form, secondary erythromelalgia (SE) has a relatively later onset and is triggered by platelet aggregation in end-arteriolar circulation (4). Currently, there is no objective criterion for the diagnosis of primary or secondary erythromelalgia (5).

Figure 1. Vasomotor changes seen in a 77 year-old patient with erythromelalgia secondary to polycythemia vera. Note the erythema and oedema present in the distal limbs. Source: Wikimedia commons

INHERITANCE

Primary erythromelalgia (PE) is an autosomal dominant trait (Online Mendelian Inheritance in Man 133020) (6). If inherited, clinical onset is early, often manifesting before the first decade of life. Linkage analysis of two separate families with PE identified the susceptibility gene to be located on 2q31-32 (7). Studies conducted on an American family with this condition identified a single amino-acid substitution (F1449V) in SCN9A, the gene encoding the voltage-gated sodium channel Nav1.7 (8-10). A number of other mutations in the same channel have also been found in other families with PE (see Dib-Hajj et al.(11) for review).

THE SODIUM CHANNEL AND ITS RELATION TO PAIN SENSATION

The SCN gene family encodes a number of related voltage-gated sodium channels (VGSC) with diverse spatial and temporal expression (See Table 1). These channels all display selectivity towards Na⁺ (12). The functional importance of these channels is seen in the context of action potential propagation (13). Depolarising stimuli that raise the membrane potential above threshold, results in an increase in the probability that the channel will be open. The mechanism behind voltage gating relates to the movement of specific charged amino-acid residues within the channel in response to a membrane electric field (14). This mechanical movement initiates an opening of the central pore of the channel, enabling diffusion of Na⁺ in the direction of its electrochemical

ABSTRACT

Chronic pain is a complex, disabling medical problem that presents constant challenges to pain specialists worldwide. Much research has been done in order to understand the molecular and functional characteristics of acquired inflammatory and neuropathic pain but little is known about the inherited pain syndromes. This review will focus on the hereditary hyperalgesia syndrome known as primary erythromelalgia. We will provide an insight into the molecular pathogenesis of this relatively unknown medical condition, outline current management strategies and discuss current research in relation to novel therapeutic options.
Milliseconds after activation of the channel, the tetrapeptide isoleucine-phenylalanine-methionine-threonine undergoes a conformational change by moving into the inner mouth of the channel, stopping the inward flow of sodium ions and activating the channel (14). Inactivation of the VGSC allows for repolarisation of the membrane potential.

Voltage-gated sodium channels (VGSCs) are central in the mechanism of pain sensation (16). In a simple model, nociceptive dorsal root ganglion neurons in the periphery respond to painful stimuli by eliciting a depolarisation of the cell membrane (16). If the depolarising stimuli are of sufficient amplitude, an action potential is initiated and propagates through the afferent neural fibers, maintained through activation of voltage-gated sodium channels. Synapses between these nociceptors and dorsal horn neurons in the spinal cord lead to impulse propagation through the spinothalamic tract and to the cerebral cortex, where pain is perceived.

**FUNCTIONAL STUDIES ON Na\textsubscript{v}1.7 AND ITS RELATION TO THE SENSATION OF PAIN**

Nav\textsubscript{v}1.7 voltage-gated sodium channels are preferentially expressed within dorsal root ganglion (DRG) neurons, sympathetic ganglion neurons (SGNs) and not expressed at significant levels in the central nervous system (18). Additionally, Nav\textsubscript{v}1.7 localises within tips of neurites of DRG neurons in culture (19). Targeting of Nav\textsubscript{v}1.7 to the nerve terminal may function to amplify the potentials received from the periphery. Perhaps the strongest evidence that links Nav\textsubscript{v}1.7 with pain perception are studies of families whose members have the rare congenital insensitivity to pain syndrome (20). Linkage analysis studies showed mutations in SCN9A, causing loss-of-function mutations to Nav\textsubscript{v}1.7 (21).

Electrophysiological studies on Nav\textsubscript{v}1.7 demonstrate that the channel displays fast activating currents and slow rate of recovery from inactivation (22). In comparison to other VGSCs, the slow rate of recovery from inactivation, thus long refractory period, makes it unlikely that Nav\textsubscript{v}1.7 significantly contributes to the battery of repetitive action potentials received from the periphery during nociception. Instead, it is likely that Nav\textsubscript{v}1.7 acts as a threshold channel by amplifying depolarising potentials generated by stimuli of the DRG neurons (22). This amplified depolarisation recruits other VGSCs (primarily Nav\textsubscript{v}1.8) to produce an action potential (22).

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Table 1. Expression and function profiles for Sodium channel alpha-subunits (17).

<table>
<thead>
<tr>
<th>Protein Name</th>
<th>Gene</th>
<th>Expression Profile</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na\textsubscript{v}1.1</td>
<td>SCN1A</td>
<td>Central neurons and cardiac myocytes</td>
<td>Action potential initiation, repetitive firing in neurons, excitation-contraction coupling in cardiac myocytes</td>
</tr>
<tr>
<td>Na\textsubscript{v}1.2</td>
<td>SCN2A</td>
<td>Central neurons</td>
<td>Action potential initiation, repetitive firing in neurons</td>
</tr>
<tr>
<td>Na\textsubscript{v}1.3</td>
<td>SCN3A</td>
<td>Central neurons and cardiac myocytes</td>
<td>Action potential initiation, repetitive firing</td>
</tr>
<tr>
<td>Na\textsubscript{v}1.4</td>
<td>SCN4A</td>
<td>Skeletal muscle</td>
<td>Action potential initiation and transmission in skeletal muscle</td>
</tr>
<tr>
<td>Na\textsubscript{v}1.5</td>
<td>SCN5A</td>
<td>Cardiac myocytes, skeletal muscle, central neurons</td>
<td>Action potential initiation and conduction</td>
</tr>
<tr>
<td>Na\textsubscript{v}1.6</td>
<td>SCN8A</td>
<td>Central neurons, dorsal root ganglia neurons</td>
<td>Action potential initiation and transmission</td>
</tr>
<tr>
<td>Na\textsubscript{v}1.7</td>
<td>SCN9A</td>
<td>Dorsal root ganglia neurons, sympathetic nervous ganglia, Schwann cells and neuroendocrine cells</td>
<td>Action potential initiation, enhances sub-threshold depolarisations</td>
</tr>
<tr>
<td>Na\textsubscript{v}1.8</td>
<td>SCN10A</td>
<td>Dorsal root ganglion</td>
<td>Contributes most to action potential in dorsal root ganglia</td>
</tr>
<tr>
<td>Na\textsubscript{v}1.9</td>
<td>SCN11A</td>
<td>Dorsal root ganglion</td>
<td>Depolarising influence to resting potential, enhances sub-threshold depolarisations</td>
</tr>
<tr>
<td>Na\textsubscript{x}</td>
<td>SCN7A</td>
<td>Cardiac myocytes, uterus, skeletal muscles, dorsal root ganglion</td>
<td>Not clearly elucidated</td>
</tr>
</tbody>
</table>
FUNCTIONAL IMPLICATIONS OF MUTATIONS IN Na\(v\)1.7 UNDERPIN THE MOLECULAR PATHOGENESIS OF PRIMARY ERYTHROMELALGIA

A number of mutations found in patients with PE have been characterised and the resultant mutant channels cloned and studied using electrophysiological techniques. The mutations that have been described have occurred as gain of function mutations in highly conserved regions of the known VGSCs (11). The altered biophysical properties of these mutant channels have been used to explain the mechanism behind the hyperalgesia in PE. Broadly speaking, patch-clamp analysis has shown that these mutations cause a hyperpolarising shift in activation of the channel (making it easier for the channel to open) and a slowing of inactivation kinetics (increasing the time that the channel stays open), accompanied by an enhanced response to small depolarising stimuli (23-25). Such biophysical changes cause hyperexcitability in the cells that express these mutant channels (23), such as DRG neurons. Furthermore, activation of mutant Nav1.7 channels close to the resting potential depolarise the neuronal cell membrane leading to activation of other VGSCs (mainly Nav1.8) that contribute to the upstroke of the action potential in these cells (23). Indeed, much lower input current amplitudes are required to generate an action potential in DRG neurons transfected with the L858H PE variant Nav1.7 channel when compared to the controls (26). This hyper excitability may result in the experience of unprovoked pain (27).

VASOMOTOR CHANGES INDUCED BY Na\(v\)1.7 MUTATIONS IN PRIMARY ERYTHROMELALGIA

Vasomotor changes characterise attacks of PE. A study conducted by Mork et al confirmed a reduced skin capillary density during attacks of erythromelalgia (28). The aetiology of this reduction in skin capillary density is hypothesised to be a result of arteriovenous shunting (28). Shunting results in insufficient blood circulating through the nutrient capillaries in the skin, which directly contributes to skin hypoxia. Decreases in oxygen delivery to the skin triggers arteriolar dilatation manifesting as erythema (29).

Littleford and colleagues (30) investigated focal sympathetic neural activity by measuring vasomotor reflexes at the toe and finger pulps, areas with dense arteriovenous anastomosis (31). Their study found that patients with erythromelalgia had diminished sympathetic vasoconstrictor responses to both cold stimuli and an inspiratory gasp (30). Indeed, it is plausible that impaired sympathetic outflow may contribute to the altered vasomotor changes that occur in attacks of erythromelalgia.

Sympathetic ganglion neurons (SGNs) express Nav1.7, but lack Nav1.8 (32, 33). Expression of L858H mutant Nav1.7 in SGNs increased the threshold for single action potentials, reduced the maximum amplitude of the triggered action potential and lowered the frequency of firing of SGNs (26). The same paper reports that expressing Nav1.8 channels in SGNs transfected with L858H mutant Nav1.7 restored wild-type behaviour in the SGNs(26). It is likely that the difference in excitability due to gain-of-function mutations in Nav1.7 channels expressed in DRG and SGNs is related to the co-expression of Nav1.8 in DRG neurons and not in SGNs (26). Nav1.8 is known to significantly contribute to the upstroke of the action potential (34) and is relatively resistant to membrane depolarisation (and thus inactivation) (26). Hence, gain-of-function mutations in Nav1.7 in SGNs lacking Nav1.8 will lead to inactivation of other VGSC that are not resistant to the membrane depolarisation afforded by PE-variant Nav1.7 channels. In this manner, PE variant Nav1.7 channels in SGNs may decrease sympathetic outflow and impair vasomotor tone as described above, whilst contributing to the hyper-excitability of DRG neurons and the sensation of unprovoked episodic burning pain that characterises PE (27).

TREATMENT AND MANAGEMENT OPTIONS

PE related to SCN9A (Nav1.7) mutations is an incurable condition that is difficult to manage (35). Conservative management includes patient education, genetic counselling, avoidance of aggravating factors, cooling techniques, controlling secondary and underlying factors, and selective medications (36,37). Perhaps the most effective conservative management for erythromelalgia is immersion of the affected limb in cold, such as ice water (38). Indeed, whole cell voltage-clamp recordings on HEK293 cells expressing the PE mutation L858F showed a cooling dependent shift of the activation midpoint of L858F to higher membrane potentials, closer to that of HEK293 cells expressing wild-type channels (39). Management strategies must also pay attention to the psychological distress of the disease, especially since the disease onset occurs in the paediatric population (40).

Currently, there are no definitive treatment options for PE. Much of the evidence comes from anecdotal studies or small case series where there is no distinction between primary and secondary erythromelalgia. Aspirin should be trialled in all cases, and is particularly effective in secondary erythromelalgia due to thrombocythaemia (41). Pain responsive to aspirin should warn the clinician of an underlying myeloproliferative disease (42). Sodium nitroprusside may be helpful in children (44). Vasoactive drugs such as beta-blockers, magnesium and ergot alkaloids have been trialled with mixed results (37). The calcium antagonist diltiazem has proven to be effective at reducing pain in some individuals (45). Neuroactive drugs have also been trialled. Vanfloxetine, a serotonin-norepinephrine reuptake inhibitor (SNRI) induced remissions in nearly a dozen individuals when used as last-line therapy (46). Gabapentin, an antiepileptic drug with known efficacy in the treatment of chronic neuropathic pain and fibromyalgia (47), has been used effectively in a small number of cases (48).
VGSC blockers should, given the molecular genetics of PE, prove effective in the treatment of this condition. Non-selective sodium channel blockers including lidocaine infusion, lidocaine patch or oral mexiletine have been used with proven efficacy in both primary and secondary erythromelalgia (49-51). Recent research has been targeted at developing novel VGSC blockers that are isoform selective. For example, antagonism of Nav1.7 may reproduce a congenital insensitivity to pain like phenotype (20). Specifically targeting this channel isoform in an effort to mimic congenital insensitivity to pain Nav1.7 loss-of-function and analgesic phenotype represents a rational treatment for PE, because it should target the underlying hyper-excitability in the DRG neurons that underlie the pathophysiology of PE. Furthermore, given the restricted distribution of Nav1.7 channels to DRG and SG neurons and away from the CNS (52, 53), it is tempting to speculate that selective antagonism of this specific isoform will yield a favourable side-effect profile. Goldberg et al. (54) studied a novel Nav1.7 blocker XEN402 in patients with confirmed clinical and molecular diagnosis of PE. The study reported a significant increase in the time to maximal pain induction and significantly reduced the amount of pain after induction (54). Whilst this study showed that XEN402 blocks Nav1.7 mediated pain in PE, the study design was hampered by lack of subject numbers (only four were included in randomisation), a short dosing period (two-days) and a lack of monitoring of adverse-effects. However, this study is the first of its kind to examine the effects of a selective Nav1.7 antagonism as therapy for PE.

Other selective Nav1.7 blockers are being developed and tested in animal models (for review see Theile and Cummins (55)). Research at Merck laboratories developed a series of novel benzazepinone-based selective Nav1.7 blockers that displayed inhibition of spontaneous neuronal firing in vivo in a rat peripheral axotomy model, as well as reversing tactile allodynia in a rat spinal nerve ligation model (56). Further developments on a series of imidazopyridine-based selective Nav1.7 blockers showed favourable efficacy in the same rat spinal nerve ligation model with an associated reversal of inflammatory pain (57).

**FUTURE DIRECTIONS IN THE THERAPY OF PRIMARY ERYTHROMELALGIA**

PE exerts a significant toll on its patients. Now that we have a molecular understanding of this condition, it is only a matter of time until suitable therapeutics are developed that target the underlying molecular abnormality. However, there is a long way to go yet before we have definitive options for this debilitating condition. For example, the pathophysiology of the vasomotor changes underlying PE is largely unknown, and different gain-of-function mutations in different regions of SCN9A produce different pain phenotypes (Table 2). It is likely that a number of factors, including cell dependent modulation of expression, epigenetic factors and environmental influences regulate the activity of normal ion channels and thus modulate the effects of Nav1.7 monogenic mutations such as in PE. Future research must address these issues in the search for definitive therapeutics for PE.

An interesting area for future research is the potential link between mutant Nav1.7 in PE and the thermosensitive sensors of the Transient Receptor Potential (TRPV) Channel subfamily. This functional link has been implicated by the knowledge that pain in PE is triggered by temperatures as low as 32-36°C, a range that is not normally enough to trigger painful sensation (11). TRPV channels are expressed in the afferent terminals of nociceptors and are activated by noxious stimuli including high heat (>43°C), low pH (<6.0) and capsaicin (59). Given that Nav1.7 channels are expressed in DRG neurons, and in particular, nociceptors neurons, co-expression of this VGSC with TRPV channels may provide a novel therapeutic target for nociceptive antagonism in PE. Further research must be done in order to elucidate the presence of Nav1.7 in these cells.

<table>
<thead>
<tr>
<th>Pain syndrome</th>
<th>Type of mutation</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE</td>
<td>Gain of function</td>
<td>Paroxysmal attacks of pain localised to distal extremities with erythema, oedema and skin warmth</td>
</tr>
<tr>
<td>PEPD</td>
<td>Gain of function</td>
<td>Paroxysmal attacks of pain and skin flushing progressing from perirectal areas to ocular, maxillary and submandibular areas</td>
</tr>
<tr>
<td>Mixed PE – PEPD</td>
<td>Gain of function</td>
<td>Mixed PE – PEPD phenotype</td>
</tr>
<tr>
<td>SFN chronic pain</td>
<td>Gain of function</td>
<td>Chronic continuous course of pain, especially distal pain, with autonomic symptoms</td>
</tr>
<tr>
<td>CIP</td>
<td>Loss of function</td>
<td>Inability to experience any pain</td>
</tr>
</tbody>
</table>

PE – Primary Erythromelalgia, PEPD – Paroxysmal Extreme Pain Syndrome, SFN – Small Fiber Neuropathy, CIP – Congenital Insensitivity to Pain.

Table 2. Clinical syndromes caused by gain-of-function mutations and loss-of-function mutations in the Na1.7 channel (58).
REFERENCES

12. Catterall WA. From ionic currents to molecular mechanisms of a functional link, if any, between the two channels. However, unrelated to this putative link is the ability to utilise the specific expression of TRPV channels to nociceptors in order to target analgesics specifically to these pain-transducing fibers (60). TRPV1 channels have large pores that are capable of passing small charged molecules, for example, QX-314, a permanently charged quaternary derivative of lidocaine, from the extracellular to intracellular compartment, where they may exert an analgesic effect specifically to the nociceptor fibers (61). This specific targeting of VGSC blockers to nociceptors has the potential of reducing systemic side effects whilst delivering effective local analgesia. Indeed, it will be interesting to review the developments of this field in regards to treatment of PE in the future.

Conflict of interest: Nil declared
The Birthplace of Chronic Disease
A Literature Review

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INTRODUCTION

The obesity epidemic is a rapidly progressing global concern (1). Obesity has a multifactorial aetiology and is the result of a complex interplay between genetic and environmental factors overlaid on variable socio-economic conditions (Figure 1) (2). In developing countries that have acquired western diets, there has been a swing in the overall health burden from under-nutrition and infection, to obesity and chronic diseases such as coronary artery disease, and type-II diabetes (T2DM) (3). In developed countries, rising obesity continues to cause increases in long-term physical, mental and psychosocial morbidities (4). In 2006 the World Health Organisation stated that there are over one billion overweight adults; at least 300 million of whom were obese (1). Obesity among children and adolescence is also an emerging problem, with a 2007 report by the Australian Government’s Standing Committee on Health and Ageing revealing that around 21-25% of Australian children are already overweight or obese (5). Moreover, childhood and adolescent obesity is increasing at an alarming rate, having risen three fold since the 1970s (5-9). This increase is also anticipated to continue unabated reaching present adult rates of obesity by 2035 (5). One major reason for this continued increase is that many strategies targeting the aetiologies of obesity have been largely ineffective to date (3). Fortunately, in recent years a promising new paradigm has emerged to tackle the obesity crisis. This paradigm is based on the developmental origins of health and disease hypothesis and emphasises the importance of environmental factors during early fetal, infant and early childhood development as a model to profoundly influence adult health (10-13).

DEVELOPMENTAL ORIGINS OF HEALTH AND DISEASE HYPOTHESIS AND FETAL PROGRAMMING

In the early 1990s, David Barker and colleagues pioneered a series of groundbreaking studies that formed the basis for the developmental origins of health and disease hypothesis or Barker hypothesis (14-19). This hypothesis states that certain human disorders stem from environmental factors experienced during fetal life that cause non-modifiable changes made to the structure and function of an individual’s organs, metabolism and genotype (20). Central to this idea is the concept of ‘developmental plasticity’. It refers to the notion that an individual’s genotype is plastic or adaptable during development, and that genotypic expression may be altered by the environmental conditions it is subjected to (21, 22). These changes do not constitute genetic sequence modifications, but rather, epigenetic modifications that can modify the expression of specific genes. Ultimately, these epigenetic changes result in variable phenotypes (30). Barker et al. suggested that the metabolic connection (through the placenta) between the mother and fetus underpinned these physiological changes to the fetus (23). From an evolutionary perspective, such physiological changes are proposed to be positive adaptations because they tended to optimise survival of the fetus (21). However, they amounted to permanent modifications in sequence expression, which were propagated throughout that individual’s life (22). This process has been coined ‘fetal programming’.

ABSTRACT

Since the inception of David Barker’s developmental origins of health and disease (DOHaD) hypothesis over 20 years ago, there has been a paradigm shift in our understanding of chronic disease. Substantial evidence has been accrued which holds that events during our early development predispose us to the development of disease in later life. Inverse relationships have been drawn between low birth weight (LBW) and high blood pressure, coronary artery disease, strokes, obesity, diabetes, and cancer. However, the DOHaD hypothesis has ramifications well beyond LBW. It also considers the predictive merit of other fetal anthropometric measures, such as large for gestational age (LGA), stressed normal birth weight (NBW), and premature babies. These measures must also be weighed within the context modifiable and non-modifiable stressors during pivotal periods of development, and its impact on disease state. This review will explore the DOHaD hypothesis and provide examples by evaluating the outcomes of different fetal anthropometric measures. Evidence is reviewed from animal, placental, singleton, and twin studies to demonstrate the DOHaD hypothesis. It is hoped this knowledge may empower health care professionals to develop population health interventions, pharmacotherapies, and environmental modifications to improve the long-term health outcomes of their patients.
THE THRIFTY PHENOTYPE HYPOTHESIS AND THE MISMATCH PHENOMENON

The pathogenesis of fetal programming, as it relates to the development of chronic disease, is a result of the ‘thrifty phenotype hypothesis’ and ‘mismatch phenomenon’. The thrifty phenotype hypothesis holds that during periods of malnutrition the fetus may undergo physiological permutations of ancillary organs to protect neurological development and promote survival (24). This might constitute a diversion of fetal blood flow and nutrient to the brain, to preserve its growth and function, while compromising other organs, such as liver, pancreas and muscle. These physiological stresses will serve to modify the fetus’ homeostatic responses to nutrition so as to develop in-utero and will prepare it for the extra-uterine environment (25). These changes are adaptive when the malnutrition experience in the uterus is matched with the malnutrition of the extra-uterine environment (25). The fetus will be able to rapidly utilise nutrients to facilitate growth in nutrient poor environments, propagating a long-term survival benefit. Conversely, when the intra- and extra-uterine environments are significantly ‘mismatched’, the adaptive advantage may be lost and can lead to diseases later in life (24). For example, in western societies impaired intrauterine growth may be superimposed on a state of nutrient abundance and high caloric diets following birth. This mismatch in nutrient availabilities and the thrifty phenotype adaptation may result in rapid nutrient utilisation, eventually leading to increased levels of adiposity later in life. More recently, fetal programming and the mismatch phenomenon have also been applied to developmental periods during early infancy and childhood (20, 26). Despite this, further research is required to elucidate the extent to which these factors will influence humans later in life when applied during early infancy and childhood.

CATCH-UP GROWTH

Many human and animal studies have also suggested that the pattern of weight gain during early life is a critical component the DOHaD hypothesis (27). One pattern of weight gain has been termed ‘Catch-up’ growth. It describes the body’s natural tendency to recover weight after a period of nutrient deprivation (27). From an evolutionary perspective, catch up growth is important for the survival of the individual and the species as it can improve reproductive potential (21). However, when applied to the DOHaD hypothesis, it can be used to predict whether an individual will be overweight later in life. For example, Ong et al. illustrated that neonates who showed catch up growth in their first two years had more central fat and total body fat at the age of five in comparison to children without catch-up growth (27). This is independent of anthropometric variables at birth. Moreover, LBW babies who undergo rapid growth rates during early childhood are at increased risk of T2DM (28). For each standard deviation increase in weight between the ages of 7 and 15, there was an odds ratio of 1.83 (CI, 1.37 to 2.45; P < 0.001) for the development of T2DM, when restricted to persons with birth weights below 3000 grams. It is not clear whether nutrient limitations during the catch-up period will prevent metabolic syndrome, but this could be an area for further research because it might be a potential target for future public health interventions.

ANIMAL STUDIES

Numerous animal studies have support-
ed the DOHaD hypothesis, using a variety of different species and interventions (29-33). Some of these studies used total, partial or selective nutrient or calorie limitation to induce different states of fetal growth restriction. Others have caused toxin exposures or performed placental micro-embolisation to induce intrauterine hypoxia, but all with the purpose of replicating intrauterine insults. For example, fetal animals exposed to under-nutrition demonstrate reduced renal volumes and nephron density, leading to hypertension and chronic renal failure later in life (34). In another animal model, rats are subjected to nutrient limitations in utero to evaluate its effect on β-cell mass and long-term glucose metabolism. Rats demonstrated a 35% reduction in β-cell mass at birth and later developed glucose intolerance as adults (35, 36). In a review by McMillen and Robinson they encapsulate the evidence of animal studies on the DOHaD hypothesis, by corroborating the experimental evidence with the observed human epidemiology found in the literature (22).

THE PLACENTA

Placental characteristics must be considered when applying the DOHaD model. The growth of a fetus is largely influenced by the ability of the mother to provide nutrients to its unborn offspring. The placenta connects the fetus to the mother and is the gateway of the nutrients required for life. It regulates nutrient transport by balancing maternal nutrient supply with fetal nutrient demands (37). Therefore, one can correlate the mass, size, shape and surface area of the placenta with its ability to deliver nutrients to the fetus (37). Subsequently, predictions about adult disease can be made based on characteristics of the placenta, in combination with the mother’s anthropometric features (38). A study of 6975 men born in Finland, between 1934-44, show that different placenta characteristics were predictive of CVD later in life. For every one centimetre increase in the difference between diameter and thickness of the placental surface, the odds ratio (OR) for CVD disease increased 1.14 (95% confidence interval 1.08–1.21, P<0.0001) (38). Similarly, every 0.4 m² decrease in the surface area of the placenta increased the OR of CVD by 1.25 (1.10–1.42, P<0.0001) (38). Placental features have been connected with elevated blood pressure, chronic heart failure, CVD, and some types of neoplasia in the offspring (38-42).

SINGLETON BIRTH WEIGHT STUDIES

Most studies looking at the DOHaD hypothesis have used birth weight as a crude measure of intrauterine growth, health and fetal nutrition with BMI being used as the measure of obesity later in life. Furthermore, it is routinely measured at birth, has established epidemiological standards, is historically available, and has been studied at various developmental intervals (3).

LOW BIRTH WEIGHTS (LBW)

Many studies have shown that low birth weights can be a marker for poor intrauterine health and an increased propensity for later adult disease (20, 43-45). For example, LBW can be indicative of impaired fetal growth, which has been linked to a variety of diseases, from hypertension and coronary artery disease to cancer and mental health problems (Table 1 (46-51)). These associations have been replicated in a variety of human and animal cohorts over the last four decades (46, 50, 52). One of the seminal studies looked at LBW and its effect on cardiovascular development (18). This effect was illustrated by a longitudinal cohort study of 6425 subjects with LBWs at four Swedish delivery units between 1925 and 1949 (53). During follow-up from 1987 to 2002, the risk of coronary artery disease was significantly higher in subjects with low birth weight in comparison with normal birth weight controls, independent of gestational age (adjusted hazard ratio 1.64, 95% CI 1.23-2.18) (53). Another study supported this association by demonstrating a link between LBW and increased aortic wall thickness (a marker for early atherosclerosis) in comparison to NBW (54). Moreover, the connection between LBW and cardiovascular disease (CVD) has now been reproduced in men and women in Europe, North America and India (55-57). Despite this and other clear associations, it is important to remember that LBW is not necessary or sufficient for chronic disease in later life (58).

LARGE FOR GESTATIONAL AGE (LGA)

Epidemiological studies have been conducted investigating LGA babies’ outcomes and each has demonstrated the existence of a direct association with obesity later in life (63-66). For example, in the 2003 ‘Growing Up Today’ Study, a cohort study of 14,000 adolescents born at full-term was investigated for evidence of the DOHaD hypothesis (57). It showed that a 1kg rise in birth weight,

<table>
<thead>
<tr>
<th>Chronic Diseases Associated with the Developmental Origins of Health and Disease Hypothesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic Syndrome – dyslipidemia, obesity, hypertension, insulin resistance</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>Kidney Disease — Glomerulosclerosis</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
</tr>
<tr>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>Bone Disease - Osteopenia and Osteoporosis</td>
</tr>
<tr>
<td>Lung abnormalities—BPD, Reactive Airway Disease</td>
</tr>
<tr>
<td>Immune dysfunction</td>
</tr>
<tr>
<td>Liver failure — Cholestasis, Steatosis</td>
</tr>
<tr>
<td>Dementia - Alzheimer’s disease</td>
</tr>
<tr>
<td>Mental Health Problems - Depression, Anxiety, Bipolar Disorder, Schizophrenia</td>
</tr>
<tr>
<td>Neoplasia</td>
</tr>
</tbody>
</table>

Table 1. Chronic Diseases that have been associated with developmental plasticity and fetal programming (45-51, 59-62).
compared to reference standards, had a ~50% increased risk of being overweight at ages 9 to 14 years (67). After adjusting for the effect of maternal BMI and additional social and economic factors, the increase in risk was 30% (67). A 1997 study with 4300 participants by Sørensen et al. further expands on this direct correlation between higher birth weight and increased BMI showing the effect is sustained into young adulthood (age of 20) (68). Sørensen et al. also demonstrated that BMI at ages 18 to 26 rose progressively over the range of birth weights, after controlling for gestational age, birth length and maternal factors (68). In addition, Venn et al. demonstrated that childhood obesity is not only correlated with adult obesity but that it actually directly accounts for around 22% of adult obesity (69).

THE U-SHAPED RELATIONSHIP

Collectively, the epidemiological evidence suggests that both high and low birth weight confers additional risk for later life obesity. Therefore, we are confronted with a paradox that adult obesity and the potential for chronic disease can occur at either end of the birth weight spectrum. McCance et al. argue that there may be a U-shaped relationship between birth weight and later life outcomes, as the DOHaD hypothesis exerts its effects in LBW and LGA babies (70).

TWIN STUDIES

Twin studies are a useful means of determining whether genetic factors or intrauterine factors play a major role in later life outcome. The effect of these factors may be studied by examining monozygotic twins (shared intrauterine environment and identical genetic makeup) and dizygotic twins (shared intrauterine environment and non-identical genetic makeup) together and in isolation. A further advantage of twin studies is that it allows comparison of anthropometric variables such as birth weight in isolation of confounding factors such as socio-economic variables, the assumption being that twins are raised in the same household under similar parentage. The largest twin study examining the relationship between birth weight and T2DM in later life found that, when examining the cohort as singletons, there was a doubling of T2DM risk for every kilogram decline in birth weight, the effect size being similar to that of normal singleton studies (71). However, a within-pairs analysis of monozygotic twins in the cohort found that a similar doubling of diabetes risk occurred in this group (71). Similarly, analysis on a Danish twin register examining 14 monozygous twin pairs discordant for diabetes showed that the diabetic twin had significantly lower birth-weight when compared to the normal co-twin (72). This effect was similarly reproduced in an Italian study examining 13 monozygotic twins who were discordant in their result for an oral glucose tolerance test – lower birth weight predicted an abnormal response (p <0.0001) (73). Ijzerman et al., in a study of 53 dizygotic and 61 monozygotic twins, showed that low birth weight was associated with insulin resistance and lower HDL in both DZ and MZ twins, with there being no difference between these groups (74). This indicates that these specific cardiovascular risk factors may be, in part, independent from genetic effects. The same study showed that LBW was associated with high blood pressure, total and LDL cholesterol, fibrinogen and sympathetic activation within DZ pairs, but not within MZ pairs (74). The conclusion drawn from this study was that certain risk factors may be associated with genetic loading whereas others are dependent on intrauterine environments (74).

Whilst these studies are interesting, they do not stratify the magnitude of effect by chorionicity. Therefore, further research must be done in order to differentiate the effect of birth weights between monochorionic monozygous twins and dichorionic monozygous twins.

CONCLUSIONS

With current remedial interventions for obesity being inadequate, a new approach to obesity management is needed (3). However, proposed interventions to modify the early life anthropometric factors and chronic diseases, such as cardiovascular disease, need to be well researched and safe. Indiscriminate efforts to modify birth weights and early life weights could be very dangerous and may cause increased rates of sequelae later in life. At any rate, the implications for modern population health preventions is that obesity prevention can begin in-utero or in early life and could result in positive lifelong or even multigenerational impact. The social, economic and health gains would also be vast. In contrast, failure to address the obesity epidemic may lead to an intergenerational cycle of obesity and chronic disease.

Acknowledgements: Nil

Declaration of Conflicts of Interest: Nil

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70. McCance DR, Pettitt DJ, Hanson RL, Jacobsson LT, Knowler WC, Bennett PH. Birth weight and non-insulin dependent diabetes: thrifty genotype, thrifty phenotype, or surviving small baby genotype? BMJ. 1994 Apr 9;308(6934):942-5.
INTRODUCTION

This case of pulmonary-renal syndrome presented a unique diagnostic dilemma, and serves as a useful platform to discuss the systemic vasculitides. Although a diagnosis of Wegener’s granulomatosis (WG) was highly probable, evidence of a coexisting anti-glomerular basement membrane (GBM) disease made for an interesting differential diagnosis. The patient presented in this case quickly developed severe and rapidly progressive renal and respiratory failure, which was ultimately fatal.

CASE REPORT

In June 2011, a 71 year-old Caucasian female presented to her regular general practitioner (GP) with a three week history of lethargy, malaise and dry cough, associated with intermittent low-grade fever and bilateral sinus pain. Significant negatives included no nasal discharge, haemoptysis or headache. Her previous medical history was unremarkable, and she was not taking any medication. She was a lifelong non-smoker, with no known allergies and no significant family history.

General examination findings were unremarkable. On ear, nose and throat (ENT) examination, bilateral sinus tenderness was present, and chest auscultation revealed only mild bibasal crepitations. Based on the clinical picture, the GP subsequently diagnosed the patient with sinusitis, and initiated a course of antibiotics. At follow-up two weeks later, the patient’s sinusitis had failed to respond to antibiotics, and a new course was commenced. At her third consultation, one week later, the patient’s sinusitis was now complicated by severe lower limb oedema, oliguria and dyspnoea. The GP immediately referred her to the emergency department (ED) of the local regional hospital, and she presented soon after.

At admission, a petechial rash on the anterior aspect of her left forearm was noted. The patient was afebrile, with a respiratory rate of 22 breaths/min, oxygen saturation of 91%, blood pressure of 180/100 mmHg and pulse of 90 beats/min. Blood tests and a chest X-ray were promptly completed. The chest X-ray revealed bilateral patchy opacities (see Figure 1).

Urea and electrolytes revealed acute renal failure, with a creatinine of 940 micromoles/L, and an estimated glomerular filtration rate (eGFR) of 4mL/min. Full blood examination demonstrated marked neutrophilia of 19x10^6/mL, and inflammatory markers responded to antibiotics, and a new course was commenced. At her third consultation, one week later, the patient’s sinusitis was now complicated by severe lower limb oedema, oliguria and dyspnoea.

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Figure 1. Chest X-ray revealed bilateral patchy opacities

Figure 1. Chest X-ray revealed bilateral patchy opacities

ABSTRACT

This case presents a 71 year old female patient who developed acute renal failure after a one month history of pansinusitis, which was unresponsive to antibiotic treatment. This was complicated by respiratory failure, requiring ventilatory support. Investigations showed the presence of circulating PR3-ANCA, which supported the diagnosis of Wegener’s granulomatosis. Further investigations showed the presence of anti-GBM antibody, and renal biopsy showed crescentic glomerulonephritis. Biopsy immunofluorescence demonstrated linear staining of capillary loops with IgM, which indicated a concurrent anti-GBM disease. Despite immunosuppressive therapy, the patient in this case rapidly progressed into respiratory failure and died on day eighteen of admission.

This report discusses such “double-positive” patients, with a brief literature review. Although serologic evidence of concurrent anti-GBM and MPO-ANCA is now well documented in the literature, there are still only a few reported cases of the unusual anti-GBM, PR3-ANCA combination.
were also elevated (C-reactive protein (CRP) 340, Erythrocyte sedimentation rate (ESR) 127 mm/hr). A jugular perma-cath was inserted for haemodialysis.

Despite the small volume of urine passed in the ED, urinalysis showed the presence of leukocytes, blood, protein, and glucose. Blood cultures were therefore taken to rule out urosepsis (and subsequently showed no growth). The patient was admitted to a medical ward and received an immediate dose of frusemide. She was also commenced on 250mg of methyl-prednisolone intravenously (IV).

A CT-scan was performed the following day and showed evidence of diffuse bilateral pulmonary infiltrates with ground-glass appearance. There were also multiple upper lobe cysts with no evidence of cavitation. There was no hilar or mediastinal lymphadenopathy and no other masses were identified (see Figure 2).

With this clinical picture, the patient received a provisional diagnosis of WG pending further investigation. Therefore, an antibody screen was ordered, including anti-neutrophil cytoplasmic antibody (ANCA), anti-nuclear antibody (ANA) and anti-glomerular basement membrane (GBM) antibody. Ultrasound-guided renal biopsy was performed to confirm a tissue diagnosis.

Over the next week, the patient continued to deteriorate, with increasing respiratory failure. On day nine of admission, she was transferred to the intensive care unit (ICU) for ongoing ventilatory support.

Serology tests returned strongly positive for both ANCA and anti-GBM antibodies, while ANA were undetected. The ANCA subtype anti-serine proteinase-3 (anti-PR3) was > 100 U/mL. Renal biopsy showed evidence of crescent formation in half of the glomeruli sampled, and glomerular necrosis in 19 out of 25 glomeruli. Biopsy immunofluorescence also showed a linear pattern of IgM staining in many glomerular capillary loops.

These results, in conjunction with the clinical picture, confirmed a diagnosis of WG, although coexisting Goodpasture’s disease was also likely. Cyclophosphamide was commenced at a dose of 200 mg/day IV with adjunctive methyl-prednisolone and supportive measures. On the eighteenth day of admission, the patient continued to deteriorate with progressive respiratory and renal failure. Further treatment was deemed inappropriate and supportive care was withdrawn.

**DISCUSSION**

Complicated by their unknown aetiology, complexity and overlap, the systemic vasculitides present a diagnostic challenge. This case highlights the importance of recognising the salient differentiating features of the vasculitides, as well as the coexistence of features of Goodpasture’s disease.

**Figure 2.** CT-chest revealed bilateral pulmonary infiltrates with ground-glass appearance and multiple upper lobe cysts

The small-to-medium vessel vasculitides include Churg-Strauss syndrome (CSS), microscopic polyangiitis (MPA) and WG, all of which are predominantly ANCA-associated vasculitides (1). The first description of ANCAs originated from Australia, where patients suffering from necrotising and crescentic GN were found to harbour antibodies that reacted with neutrophilic granulocytes by indirect immunofluorescence staining. ANCA subtypes have since been used to characterise the disease process (2, 3). WG is frequently associated with autoantibodies directed against cytoplasmic antigens (c-ANCA), specifically against serine proteinase-3 (PR3-ANCA).

As described in the case report, the presence of PR3-ANCA is a useful diagnostic tool in patients suspected of having WG. On the other hand, CSS and MPA are commonly associated with perinuclear autoantibodies (p-ANCA), which are directed against myeloperoxidase (MPO-ANCA) (2). However, ANCA results cannot definitively differentiate WG from MPA, as approximately 5% of patients with WG exhibit p-ANCA with MPO specificity (4).

Therefore, the clinical picture is an important consideration when making a diagnosis. Non-specific constitutional symptoms are a hallmark of all of the vasculitides, and may include lethargy, fatigue, myalgia, fever, anorexia and weight loss (5). It is important to note that each form of small-to-medium vessel vasculitis carries a spectrum of symptoms, and virtually any organ system may be affected.

WG is characterised by a necrotising granulomatosis of both the upper and the lower respiratory tract, with glomerulonephritis completing the triad (5). It is a rare disease, with an incidence of 3-14 cases/million (6). Without treatment, the average survival rate is approximately five months from diagnosis, which emphasises...
In a single-centre United Kingdom study of 954 ANCA-positive patients, serology showed 5% also had detectable anti-GBM antibodies (11). This study also showed that 82% of double-positive patients had anti-MPO specific p-ANCA. Pulmonary haemorrhage occurred in 44% of double-positive patients, and 68% of patients were dialysis-dependent at presentation. Although a different demographic to this case, a large study of double-positive Chinese patients revealed very similar results and an overall poor prognosis (12).

The present case report is therefore unusual, as it demonstrates a patient with a c-ANCA pattern of staining who developed anti-GBM antibodies. Similar cases of rapidly progressive pulmonary-renal syndrome in c-ANCA positive, anti-GBM positive 68 year old and 73 year-old Caucasian females have also been reported (13, 14).

A proposed mechanism for this phenomenon is that damage and exposure of renal tissue secondary to increased inflammation elicits an immune response against the GBM (15). This exposure of the GBM is thought to lead to the production of anti-GBM antibodies, which results in the development of Goodpasture’s disease.

Finally, the implications for prognosis and treatment must also be considered, given the importance of treating anti-GBM disease with plasma exchange, and its relatively poor response to immunosuppressive therapy. The UK study cited previously also demonstrated a significantly worse outcome for double-positive patients. None of the patients that were dialysis-dependent at presentation recovered renal function, despite immunosuppression.

This is in sharp contrast to patients with pure ANCA-associated vasculitis, in whom 75% of those that present dialysis-dependent will recover renal function with immunosuppression (16). Patients who present in renal failure due to pure anti-GBM disease rarely recover renal function (17). This study therefore indicates that the outcome of double-positive patients is similar to patients with pure anti-GBM disease.

CONCLUSION

This patient’s diagnosis of c-ANCA positive WG was complicated by the presence of anti-GBM antibodies. A brief literature review reveals the overall poorer prognosis for such double-positive patients, which may have contributed to the rapid progression of this patient’s illness. This case also indicates the need for new avenues of treatment, given the poor response to immunosuppressive therapy.

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Consent Declaration: Informed consent was obtained from the patient for publication of this case report.

Conflict of Interest Declaration: None
REFERENCES

Here we present the case of a 43 year old patient, and long term substance abuser, with a 925mg daily caffeine consumption (7.1 litres diet-coke®) who developed rhabdomyolysis.

INTRODUCTION

Rhabdomyolysis has many causes including drugs and toxins, trauma, muscle ischaemia, intense exercise, prolonged immobilisation, infection, electrolyte and endocrine abnormalities, genetic defects, connective tissue disorders and temperature extremes (1, 2). Drugs and alcohol are the most common cause, accounting for 81% of cases with over 150 known causative drugs (1). One such drug is caffeine and, despite its widespread use within society, there have only been a handful of reported cases of caffeine-induced rhabdomyolysis worldwide (3-9). This may be in part because substantial quantities of caffeine must be consumed to reach a toxic dose (20mg/kg) with average daily dosing ranging from 3 – 7mg/kg (10-13). Moreover, most caffeine-induced rhabdomyolysis cases have involved massive overdoses within or near the lethal 5-10 gram range (150 – 200mg/kg) (1, 3-6, 9), with only two cases occurring near the lower toxic dose threshold (7, 8). These past case reports are summarised in Table 1. We present here the first known case of caffeine-induced rhabdomyolysis within Australia, and the third reported case worldwide occurring at a near-toxic caffeine dose.

CASE REPORT

A 43 year old female patient, with a history of substance abuse, presented to the emergency department with a 12 hour history of weakness, lower limb myalgia, fatigue and an episode of passing orange-brown urine 2 hours prior to admission. This occurred on a background of 925mg daily caffeine intake (18.5mg/kg), taken as 7.1 litres or 20 cans Diet Coke® daily, every day, over the preceding 4 weeks. Additional symptoms included anorexia, nausea, intermittent insomnia and palpitations. The patient denied syncope, seizures, fever, emesis, trauma, strenuous exercise and recent illicit drug or alcohol use.

<table>
<thead>
<tr>
<th>Case Report</th>
<th>Caffeine Dose Ingested</th>
<th>Method of Overdose</th>
<th>Additional factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrenn, Et al.1989</td>
<td>3.57 g</td>
<td>Caffeine tablets (Magnum 357®)</td>
<td>–</td>
</tr>
<tr>
<td>FitzSimmons, Et al.1997</td>
<td>3.5 g</td>
<td>Caffeine tablets (non-specified)</td>
<td>excessive exercise</td>
</tr>
<tr>
<td>Kamijo, Et al.1999</td>
<td>3.6 g*</td>
<td>Oolong tea</td>
<td>15 litres fluid</td>
</tr>
<tr>
<td>Emohare, Et al.2006</td>
<td>1.6 g</td>
<td>Caffeine-rich gum</td>
<td>–</td>
</tr>
<tr>
<td>Chakraborty, Et al.2007</td>
<td>17.5 g</td>
<td>Caffeine tablets (Pro-plus®)</td>
<td>–</td>
</tr>
<tr>
<td>Mortelmans, Et al.2008</td>
<td>1.17 g</td>
<td>Diet Coke®</td>
<td>9 litres fluid</td>
</tr>
<tr>
<td>Mahapatra, Et al.2010</td>
<td>15 g</td>
<td>Caffeine tablets (Pro-plus®)</td>
<td>–</td>
</tr>
</tbody>
</table>

*Caffeine content of Oolong tea estimated (26).

Table 1. Case Reports of Rhabdomyolysis due to Caffeine Overdose (3-9).

Figure 1. Myoglobinuria observed in a person with rhabdomyolysis. Photo by James Heilman, MD. File available under the Creative Commons Attribution-Share Alike 3.0 Unported licence.
liver damage and slightly elevated blood glucose. The patient's full blood count, clotting factors, troponin, iron studies, and thyroid function tests were unremarkable. Arterial blood gas results revealed a slight metabolic acidosis. Urinalysis revealed myoglobinuria, a pH of 5.5, 3+ protein, 3+ blood and 1+ glucose. Toxicology screen, electrocardiogram, chest x-ray, and Doppler ultrasound of the deep veins in the legs were all unremarkable. The patient was diagnosed with Rhabdomyolysis with acute renal failure due to the elevated creatine kinase, classical triad of myalgia, weakness and myoglobinuria and worsening renal function tests. Management of the patient's renal failure involved intravenous crystalloid with oral rehydration fluid over 72 hours while undergoing central venous monitoring. Hypokalemia was corrected by intravenous potassium replacement. The patient was advised to cease drinking excess caffeine to prevent recurrence.

Past medical history included longstanding depression and lower back pain, as well as stage 2 kidney-disease and alcohol-induced peripheral neuropathy. Past substance abuse included opioid and alcohol abuse, ceasing three years prior following an episode of multiple organ failure (hepatic, renal and cardiac) attributed to the substance abuse. At its peak, the patient took 100 Dige- sesic® tablets (3.25 grams dextropropoxyphene and 32.5 grams paracetamol) and 165 grams of ethanol daily, every day, for 10 years. Caffeine consumption had been 300-400mg daily for many years and began increasing three years ago to reach a peak of 925mg caffeine daily, four weeks prior to admission. The patient denied illicit drug and alcohol use or abuse of prescription drugs during the past three years. The patient considers herself “happy and healthy”, having stable employment, and strong social supports including her husband, brother, two elder daughters, close friends and regular general practitioner who were all aware of her substance abuse history. The patient’s current medications included 40mg Oxycodone collected daily from a pharmacy, and diazepam p.r.n which she rarely used. Her allergies included Clarithromycin and Promethazine.

On arrival, her vital signs were a blood pressure of 120/72 mmHg, a pulse of 118 beats per minute, a respiratory rate of 30 breaths per minute, a temperature of 37.0°C and an oxygen saturation of 99 %. Abnormalities on physical examination included irritability, pallor, a fine resting tremor, twitching, fasciculations, reflex hyperexcitability, 2/5 strength in both legs, and 4/5 strength in the left arm. No other signs were found on neurological, cardiorespiratory and gastrointestinal examinations.

Investigations, summarised in Table 2, revealed a raised creatine kinase of 11,400 U/l [60-400]. Additional abnormal results included electrolyte abnormalities, moderate renal failure, liver damage and slightly elevated blood glucose. The patient’s full blood count, clotting factors, troponin, iron studies, and thyroid function tests were unremarkable. Arterial blood gas results revealed a slight metabolic acidosis. Urinalysis revealed myoglobinuria, a pH of 5.5, 3+ protein, 3+ blood and 1+ glucose. Toxicology screen, electrocardiogram, chest x-ray, and Doppler ultrasound of the deep veins in the legs were all unremarkable.

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<table>
<thead>
<tr>
<th>Caffeine Source</th>
<th>Amount of caffeine per tablet, 100ml, or 100g.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brewed coffee</td>
<td>56 – 100 mg /100 ml</td>
</tr>
<tr>
<td>Instant coffee and tea</td>
<td>20 – 73 mg / 100 ml</td>
</tr>
<tr>
<td>Carbonated sodas</td>
<td>9 – 19 mg / 100ml*</td>
</tr>
<tr>
<td>Energy drinks</td>
<td>14 – 31 mg /100ml</td>
</tr>
<tr>
<td>Chocolate</td>
<td>5 – 80 mg / 100g</td>
</tr>
<tr>
<td>Nodoz tablet</td>
<td>100 mg</td>
</tr>
</tbody>
</table>

*Diet Coke® contains 13mg/100ml.

Table 3. Caffeine content within common beverages, foods and pharmaceuticals (3,10-13).
and discharged on day four once creatine kinase had returned to within the normal range and renal function had returned to its normal level for this patient.

DISCUSSION

Caffeine is a methylxanthine available in a wide range of beverages and pharmaceuticals as summarised in Table 3 (3, 10-13). It is rapidly absorbed with a maximum plasma concentration reached 5-90 minutes following ingestion and has a half life on average of 4.9 hours (3). Metabolism of caffeine occurs predominantly in the liver via cytochrome P-450 isozyme CYP 1A2, with renal excretion of the active and inactive metabolites (14). The toxic and fatal doses of caffeine are 20mg/kg and 150-200mg/kg respectively, although doses in excess of 50g have been survived (13, 15-17).

Caffeine acts through two primary mechanisms. Firstly, it competitively antagonises adenosine receptors to promote catecholamine release, which activates postsynaptic β-adrenergic receptors (13). Secondly, it inhibits phosphodiesterase, which prevents cyclic adenosine monophosphate (cAMP) breakdown, a postsynaptic β-adrenergic receptor stimulant (13). Both mechanisms enhance adrenergic tone causing a variety of downstream effects (13). Beneficial effects occurring at low doses include heightened arousal, improved mood and improved cognition (13). Adverse effects occur as the dose increases, originating in the brain (insomnia, restlessness, tremor, reflex excitability, tinnitus, irritability, lethargy, increased respiratory drive), gut (nausea, vomiting, gastroesophageal reflux, appetite suppression), heart (palpitations, tachycardia, increased cardiac output, blood pressure alterations), kidneys (diuresis), and muscle tissue (twitching and fasciculations) (1, 2, 13, 18). Life-threatening complications of caffeine overdose include ventricular arrhythmias, seizures, severe hypokalaemia, rhabdomyolysis, acute renal failure and respiratory failure, although each typically occurs only after ingesting doses well beyond the toxic threshold (3, 4, 8, 9, 15-17, 19, 20). These complications all occur through increased adrenergic tone (as detailed in the review by Babu (2008)) with the exception of rhabdomyolysis (13).

Caffeine-induced rhabdomyolysis is proposed to occur through stimulation of intracellular calcium stores in myocytes causing tetanic contractions which induce muscle injury (4, 21). An alternative mechanism is rhabdomyolysis due to muscle paralysis occurring as a result of severe hypokalaemia (hypokalaemic muscle paralysis) (4, 19). Hypokalaemia, as observed in this case report, may have occurred through a number of mechanisms: (1) caffeine stimulation of sodium-potassium ATPase leading to hypokalaemia, (2) caffeine induced kaliuresis through increased adrenergic tone acting on the renal tubular system and (3) hypokalaemia as a side-effect of caffeine induced vomiting (4, 9, 13, 19). A third mechanism for rhabdomyolysis in this case may have been caffeine’s ability to increase muscle activity through muscle twitching, fasciculations and irritability, although how much this contributes is speculative (9).

Three factors support the proposal that caffeine was the major cause of this patient’s rhabdomyolysis. Firstly, the patient showed signs and symptoms of caffeine-induced toxicity including neural (irritability, fatigue, insomnialness, restlessness, tremor, reflex excitability, increased respiratory rate), gut (nausea, anorexia), cardiac (palpitations, tachycardia), renal (acute renal failure) and muscle tissue (muscle twitching, fasciculations) effects. Secondly, plasma caffeine levels would most likely have built up over time due to the constant daily caffeine loading, reduced metabolism from the patient’s diminished liver function and reduced excretion from the patient’s pre-existing renal failure. Thirdly, alternative causes of rhabdomyolysis were less likely; drugs and toxins (negative toxicology screen and history taking), metabolic causes (lack of severe electrolyte derangements and normal thyroid function tests), muscle ischaemia (nii clinical indications), infections (due to white cell count and presentation), and finally a lack of evidence of trauma, excessive muscle use, prolonged immobilisation, fever, hypothermia and heritable defects (2). The lack of a muscle biopsy meant an underlying muscle disorder may have been present, however. This may have accounted for the muscle injury occurring at the comparatively low caffeine dose compared to most previous studies (1, 3-6, 9). Finally, another factor that may have contributed to rhabdomyolysis in this patient is hyponatraemia from acute water intoxication due to the daily consumption of 7.1 litres of fluid (22). This mechanism is outlined by Korzets Et al, (1996) and further supported by two case studies in which 9 and 15 litres of fluid were consumed along with a caffeine overdose (6, 8, 22).

Regardless of the mechanism, our case study involved a classical presentation of rhabdomyolysis with markedly elevated creatine kinase, and the classical triad of myalgia, weakness and myoglobinuria (2). Further clinical indicators of rhabdomyolysis also observed in this case included hypokalaemia, metabolic acidosis, hyperglycaemia, and hypocalcaemia (13).

Management should be considered in all adults who have ingested a toxic dose of caffeine (3). In this case, intravenous fluid was given to correct acute renal failure and maintain renal output, while potassium supplementation was required to correct for the hypokalaemia (3). Acute renal failure, resulting from rhabdomyolysis, develops due to acute tubular necrosis as a result of toxicity from myoglobin, obstruction with precipitated uric acid and ferrirhemate and haemodynamic derangements due to vasoconstriction (9). As renal failure in this case was moderate (eGFR of 35 ml/mm/1.73 m2), and without serious metabolic derangements, renal replacement therapy was considered unnecessary (23). Management of agitation with diazepam was also considered, and intravenous lorazepam or phenytoin would have been administered had seizures occurred (3). Cardiac monitoring was conducted due to the risk of ventricular arrhythmias and if this had occurred, chemical or electrical cardioversion may have been required. Finally, gastric lavage and activated charcoal are useful for life threatening overdoses and if within one hour of ingestion (24, 25).
INTRODUCTION

On October 13, 2011 Health Care Without Harm (HCWH), an international alliance that endeavours to reduce the healthcare sector’s harm to both human and environment health, released the *Global Green and Healthy Hospital Agenda* (GGHHA) (1). In the official release, HCWH reported that the agenda aims to support existing efforts to promote and ensure sustainability and environmental health in healthcare, strengthening health systems around the globe (1). The agenda aims to do so by providing a thorough, evidence based framework that focuses on ten primary goals ranging from reducing waste production to encouraging green hospital design. It appears as though the GGHHA is to the health sector what the United Nations (UN) Millennium Development Goals (MDGs) are to global development.

THE PROBLEM

As future healthcare professionals, medical students are bound by the well-known ethical principle that we should *first do no harm* in the treatment of our patients. HCWH highlights the need to broaden this principle; the need to include a global view of health, with an emphasis on environmental sustainability (1). One of the primary motivations for the development of an agenda such as the GGHHA is the paradoxical nature of healthcare’s contribution to deteriorating environmental health. Whilst working to deal with the effects of a changing environment, the health sector continues to contribute to it through everyday operation. For example, the National Health Service (NHS) of England has calculated its annual carbon footprint to be 18 million tonnes, which is equal to 25% of total public sector carbon emissions (2). Of major concern is the degree to which the health sector contributes to global environmental disruption through service delivery, natural resource consumption and waste generation. Despite this, the GGHHA maintains a positive outlook towards the rapidly expanding availability and adoption of solutions, and the increasingly active advocacy role of those in healthcare promoting public environmental health (1).

THE OPPORTUNITY

As the environmentally minded may be aware, there have been numerous attempts in the past to promote the *greening* of our hospitals, but it is not until now that a program has been launched to unify global goals and solidify disconnected efforts. Previously, the World Health Organisation has released a document titled *Healthy Hospitals, Healthy Planet, Healthy People*, which primarily aimed to address climate change in healthcare settings (3). This has been augmented through country specific plans such as those released by Doctors for the Environment Australia (DEA) and multiple other organisations around the world (4).

In the initial release of the GGHHA, the report’s authors state that the health sector makes up approximately one tenth of the global gross domestic product (GDP) and in a number of countries has both huge economic influence and great environmental impact capable of having a detrimental effect on human health (4). Optimism is maintained, however, as they report many hospitals around the globe are leveraging this economic position in combination with their moral standing to engage sustainability, health equality and improvements in environmental health (1). In keeping with this, hospitals and health organisations from numerous countries around the globe have already joined the virtual network of participating institutions as founding members of the GGHHA. Amongst these founding members is the NHS Sustainable Development Unit (SDU), one of the world’s most prominent influences in environmentally conscious healthcare operation (1, 5).

THE GOALS

At the foundation of the GGHHA are ten interconnected goals, each containing action items that hospitals and health systems can implement to work toward more sustainable operation. Provided alongside each goal is a list of suggested actions and selected resources to assist with achieving them (Table 1).

THE FUTURE

At present, environmental sustainability in the Australian healthcare system appears lacklustre when viewed in light of the progressive NHS SDU. Specific publications detailing the current situation in Australia have been released by both DEA and Curtin University and offer practical points for action which are applicable to both the Australian and international healthcare systems (3, 6). The Evaluation and Quality Improvement Program 5th Edition (EQuIP5), prescribed by the Australian Council on Healthcare Standards, is a set of both mandatory and suggested criteria that are used in the registration of Australian healthcare
facilities. The EQuIP5 has the potential to be a strong source of intervention to ensure a lesser environmental impact of the Australian healthcare system, however, currently the criteria do not mandate any level of environmental efficiency (7, 8). The prominent reputation of the NHS SDU places it in the ideal position to influence reform of policy, such as Australia’s EQuIP5, to ensure change of practice to reflect the GGHHA goals.

There are many conservative measures that can be implemented to assist in lowering the carbon footprint of the Australian health system requiring minimal to no infrastructure or system change. For example, it has been shown that one of the simplest measures to reduce the environmental footprint is in fact increased investment in primary care (9). In this circumstance, the enhancement of preventative medicine leads to a decrease in morbidity and hence a reduction in the reliance on resource intensive curative medicine.

CONCLUSION

Over recent years, medical professionals and students alike have heard without reprieve that climate change is one of the greatest barriers to achieving and maintaining human health that the global population has collectively faced (10). The Australian Medical Student’s Association, especially, has placed great emphasis on raising awareness of this, reiterating the notion that climate change is the biggest global health threat to the 21st century (11).

Given the increasing weight that is being given to environmental sustainability in global design and operation in an attempt to address climate change, it seems appropriate that this should extend to include the global healthcare system. Although numerous frameworks for improving the environmental impact of our hospitals exist, we cannot underestimate the vital importance of a global effort that not only addresses all major environmental impacts of healthcare globally, but also provides practical actions, resources and tools to assist with achieving these goals. With major players in the international sustainability game having already committed to work towards achieving the goals outlined in the GGHHA, it seems that this framework could be the unifying impetus the international healthcare community requires to make a concerted and collective effort to honour a truly integrated approach to first do no harm.

Acknowledgements: Nil

Table 1. Global Green and Healthy Hospital Agenda goal summary (1).

<table>
<thead>
<tr>
<th>Goal</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leadership</td>
<td>Prioritise environmental health as a strategic imperative</td>
</tr>
<tr>
<td>Chemicals</td>
<td>Substitute harmful chemicals with safer alternatives</td>
</tr>
<tr>
<td>Waste</td>
<td>Reduce, treat and safely dispose of healthcare waste</td>
</tr>
<tr>
<td>Energy</td>
<td>Implement energy efficiency and clean, renewable energy generation</td>
</tr>
<tr>
<td>Water</td>
<td>Reduce hospital water consumption and supply potable water</td>
</tr>
<tr>
<td>Transportation</td>
<td>Improve transportation strategies for patients and staff</td>
</tr>
<tr>
<td>Food</td>
<td>Purchase and serve sustainably grown, healthy food</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>Prescribe appropriately, safely manage and properly dispose of pharmaceuticals</td>
</tr>
<tr>
<td>Buildings</td>
<td>Support green and healthy hospital design and construction</td>
</tr>
<tr>
<td>Purchasing</td>
<td>Buy safer and more sustainable products and materials</td>
</tr>
</tbody>
</table>

REFERENCES


Declaration of Conflicts of Interest: Nil
Autism as a ‘desirable diagnosis’ - ‘correcting’ a sex bias?

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There has been much talk about the increasing prevalence of autistic disorder and autism spectrum disorders in recent years. This has centred on discussion of whether the condition is actually increasing in our society, and what might be causing this, versus the perception that it is being over-diagnosed. Although the cause of this increase remains unclear, one thing not disputed is a strong preponderance for the male gender.

Research has demonstrated the increase in diagnosis generally, but little has specifically addressed possible change in the male to female (M:F) ratio of those diagnosed. Fombonne examined a number of previous studies and found a strong increase in autistic disorder; from a median rate of 4.4/10 000 for studies published between 1966 and 1991 to 12.7/10 000 between 1992 and 2001 (1). In a recent study comparing Western Australia (WA) and Denmark, Parner et al. found a prevalence of 35.0 and 21.1 per 10 000 births for WA and Denmark respectively for children born in 1998 or 1999. This was up from 31.9 and 19.5 per 10 000 for children born in the 1994-1995 time period (2). Large differences in prevalence between studies have been attributed to a number of reasons including diagnostic criteria used, country, age of diagnosis and rurality (where there may be less diagnosis and acceptance) (3). In Parner’s study some of the large differences may be attributed to different diagnostic criteria being used and possible environmental or biological reasons for a higher rate in WA, but it also raises the question of whether an autism diagnosis is more accepted or even sought after in Australia.

Anecdotal feeling among some paediatricians is that the current autism epidemic is due to over-diagnosis, often due to parental wishes. In Australia an autism diagnosis brings greater financial support, the importance of which is not disputed for children with increased care and medical services needs. However, this, and perhaps a sense of alleviated guilt that may come from a ‘reason’ for a child’s difficult behaviour, may lead to parents pushing for an autism diagnosis when perhaps it may not be appropriate. The concern expressed by some is that this label will be a burden throughout the life of these unclear cases and that the current trend of autism being a ‘desirable diagnosis’ will be looked back on negatively.

If we assume that the increased M:F ratio is a natural sex bias (with the quoted ratio usually lying somewhere between 3:1 and 4:1) the question then arises of what a trend for over-diagnosis may do to this ratio (4, 5). Unfortunately most studies have been concerned with the increased prevalence alone and take the sex bias as a given so do not examine it directly. Parner’s study does show a fall over time in the proportion of those diagnosed who were male in both regions; in WA this went from 88% to 81% (2).

Is this the effect that we might expect over-diagnosis to have on the M:F ratio? It has been suggested that clinicians may be less likely to diagnose a girl with autistic disorder because of the known gender difference and thus this difference may be self perpetuating (4). However, autistic disorder includes in its characteristics a lack of empathy and difficulties with social interaction, including a reluctance for physical closeness; perhaps our society would find this lack of certain socially appropriate attributes in a female to be more abnormal. Thus, it might be expected that girls displaying these features are more likely to be diagnosed than boys may be.

Further, should we assume that the historically recognised increased M:F ratio is a true sex ratio or is it a reflection of the characteristics held in common by both males and diagnostic criteria for autism? It is generally accepted by society that girls will be more caring and have less disruptive behaviour and although this is often unfairly exaggerated it is usually thought that ‘normal’ behaviours exhibited by boys and girls will differ. Does it then make sense for the same criteria to be applied to a young boy and girl being assessed for autism? Just as there are different growth charts for males and females, should there be different projections for their behavioural development? In an age where an autism diagnosis is almost trendy, and thus increasing in prevalence, clear gender appropriate diagnostic criteria are perhaps even more important.

REFERENCES

Prevention of Bordetella pertussis infection in the Australian community

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INTRODUCTION

Pertussis, also known as whooping cough, is an acute respiratory condition caused by the Gram negative bacillus Bordetella pertussis. It is highly contagious (1). When untreated, Bordetella pertussis spreads via respiratory droplets to 80% of the susceptible household contacts of the infected individual (2,3).

The typical disease progression in children is an initial irritating cough that gradually becomes paroxysmal (4). Paroxysms are characterised by repeated violent coughs that are followed by a high-pitched inspiratory whoop (4). The cough can last for up to three months or longer, and may include cough-associated vomiting and significant weight loss (5). The clinical presentation varies in adults (5).

Whooping cough is the most common vaccine preventable disease in Australia (3). Death from pertussis infection is usually the result of pertussis pneumonia, which can be complicated by seizures and hypoxic encephalopathy (5). The maximal risk of infection and severe morbidity occurs before infants are old enough to have received at least two vaccine doses (3).

The worldwide incidence of whooping cough has been estimated at 48.5 million cases and nearly 295,000 deaths per year (6). However, fatality from whooping cough is relatively rare in Australia (4).

According to the Australian National Notifiable Diseases Case Definitions published by the Australian Government Department of Health and Ageing (7), a confirmed case of pertussis requires either:
- laboratory definitive evidence; OR
- laboratory suggestive evidence and clinical evidence; OR
- clinical evidence and epidemiological evidence (7).

The requirements for laboratory definitive evidence are:
- isolation of Bordetella pertussis OR
- detection of Bordetella pertussis by nucleic acid testing (7).

The requirements for laboratory suggestive evidence are:
- seroconversion or significant increase in antibody level or fourfold or greater rise in titre to Bordetella pertussis in the absence of recent pertussis vaccination; OR
- single high IgA titre to whole cells; OR
- detection of Bordetella pertussis antigen by immunofluorescence assay (7).

By comparison to the confirmed case criteria, these case definitions state that probable cases of pertussis require clinical evidence alone (7). Both confirmed cases and probable cases are notifiable to the local Public Health Unit (7).

ABSTRACT

The incidence of Bordetella pertussis infection in Australia has dramatically increased since 2007, beyond levels that could have been reasonably projected from the cyclical pattern of outbreaks over the last two decades. Whooping cough rates are rising in most States and Territories, in both children under 10 and in the middle aged Australians who care for them.

National pertussis prevention is already well established in Australian Government policy. A vaccination is freely-available, financial incentives are in place for both doctors and parents to immunise children, and there are national guidelines for the management of whooping cough outbreaks by local public health units.

However, these traditional policies require updating as the community faces new challenges in the prevention of pertussis. Some strains of Bordetella pertussis have developed resistance to the current vaccine. Parents who conscientiously object to immunising their children against whooping cough are increasingly expressing their concern in the public arena. The pertussis infection rate among adolescents and adults, who act as a hidden reservoir for the bacterium, is dramatically increasing.

These emerging issues in whooping cough prevention require novel policy solutions. These may include developing a new vaccine, actively addressing conscientious objection, listing booster injections for adults on the Pharmaceutical Benefits Scheme (PBS) and increasing public awareness about the signs and symptoms of whooping cough.

PATTERNS OF BURDEN OF BORDETELLA PERTUSSIS INFECTION IN AUSTRALIA

In most developed nations, community-wide whooping cough outbreaks typically occur cyclically every three to four years (8), irrespective of vaccination levels (9). This is true of infection rates in Australia over the last two decades, with infections...
The incidence of whooping cough in the Australian community has dramatically increased over the last 10 years, and in particular since 2007. This increase is beyond that of normal cyclical increases. It is reflected in the number of reported cases of Bordetella pertussis infection across most states and territories, most obviously in South Australia. The only exceptions to this trend are Tasmania and New South Wales, where the incidence of whooping cough fell slightly from 2009-2010, after steadily climbing from 2007-2009 (Table 1).

In 2010, the highest incidence of whooping cough infection was among children aged 5-9 years old, closely followed by the 10-14 age group, and then the 0-4 age group. There was also a spike in infection numbers in adults aged 40-44.

Children with whooping cough experience a much more severe version of the illness than their adult counterparts (1). In particular, children younger than 6 months of age are at a much higher risk of complications and death from the disease than older children and adults (1).

Bordetella pertussis infection in the community has been observed to follow a seasonal pattern, with a greater number of infections occurring in the spring and summer months, between August and February (4). Data reported to the National Notifiable Diseases Surveillance System (NNDSS) on whooping cough in the last 5 years (Table 2) supports these findings.

### Measures Currently in Place for the Prevention of Whooping Cough

The Australian Government and the medical profession already have a number of beneficial policies in place that attempt to prevent outbreaks of whooping cough in Australian children (Table 3). However, the recent increase in the incidence of whooping cough, beyond what could have been reasonably predicted from normal cycles of outbreak, indicates a need for further policy intervention.

### Conclusion

Whooping cough is the most common vaccine-preventable disease in Australia, and infections rates are on the rise. The increases in incidence over the last three years per 100,000 population spiking in 1997, 2001 and 2005.

<table>
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<td>123.3</td>
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Table 1. Incidence of Bordetella pertussis infection across States and Territories in the last 10 years (notification rates per 100,000 population)

From the National Notifiable Diseases Surveillance System data (10)

<table>
<thead>
<tr>
<th>Year</th>
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<th>Feb</th>
<th>Mar</th>
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<th>June</th>
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<td>54.4</td>
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<td>202.3</td>
<td>259.0</td>
<td>284.5</td>
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Table 2. Seasonal trends in Bordetella pertussis infection in Australia
Table 3. Strategies for the prevention of whooping cough in Australia

<table>
<thead>
<tr>
<th>Prevention category</th>
<th>Prevention strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primordial (avoiding the emergence and establishment of the social, economic, and cultural patterns of living that are known to contribute to an elevated risk of disease)</td>
<td>The National Immunisation Committee (NIC) and the Australian Technical Advisory Group on Immunisation (ATAGI) – The NIC and the ATAGI monitor the Immunise Australia Program to ensure that the whooping cough vaccine and other vaccines in the program are administered according to the best available evidence, and that the community vaccination approach is working.</td>
</tr>
<tr>
<td></td>
<td>The Pharmaceutical Benefits Advisory Committee (PBAC) – The PBAC evaluates the clinical appropriateness and cost-effectiveness of funding the whooping cough vaccine through the Immunise Australia Program. It is responsible for considering government funding of vaccination for age groups other than those already listed on the schedule (11).</td>
</tr>
<tr>
<td></td>
<td>The General Practice Immunisation Incentive (GPII) – the GPII provides financial incentives to general practitioners for monitoring, promoting and providing appropriate immunisation to children under seven years of age (12). Practices receive payments when at least 90% of patients under the age of seven years are completely up to date with their vaccinations (13). This encourages GPs to educate their patients about whooping cough and its risk factors; to promote the benefits of immunisation, particularly to parents who are concerned about adverse outcomes; and to install recall/reminder systems that will pick up patients who are overdue for a whooping cough booster.</td>
</tr>
<tr>
<td></td>
<td>The National Immunisation Program (NIP) Schedule and the Immunise Australia Program – Whooping cough vaccine is on the NIP Schedule. This ensures that State and Territory governments purchase the acellular pertussis vaccine (DTPa) and distribute it to general practices and other immunisation providers free of charge (14). Individual children are given the vaccine progressively at two, four and six months, or on a catch-up program if they miss a dose. Booster doses are administered at four years and at 15-17 years (school based programs) (15).</td>
</tr>
<tr>
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<td>Linking of Centrelink payments to vaccination status – Receipt of two Centrelink payments, the Maternity Immunisation Allowance (MIA) and the Child Care Benefit, are linked to the vaccination status of children according to the NIP Schedule, which includes the whooping cough vaccine. The linking of MIA and vaccination status promotes the completion of the whooping cough booster vaccination at four years of age. It is noted that a limitation of this measure is that parents who register as conscientious objectors to vaccination are still eligible for the payments (16).</td>
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<td>Medicare Benefits Schedule (MBS) item for vaccination – the Australian Government subsidises individual private consultations which involve immunisation through the MBS. In combination with the PBS listing of vaccines, this makes it possible for all Australians to gain access to the whooping cough vaccination (14).</td>
</tr>
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<td></td>
<td>The Australian Childhood Immunisation Register (ACIR) – the ACIR is a national register of government-funded vaccinations given to children under seven years of age. Parents and health care providers can contact the ACIR to find out their child’s immunisation status at any time, which promotes timely vaccination. (17).</td>
</tr>
<tr>
<td>Secondary (curing patients and reducing the more serious consequences of disease through early diagnosis and treatment)</td>
<td>Antibiotic treatment – patients with whooping cough are immediately treated with either azithromycin for five days, or erythromycin or clarithromycin for seven days (18). Antibiotic treatment provides the greatest reduction in symptoms when given early in the illness (19). The Series of National Guidelines – Pertussis (SoNG) (18), the Pertussis National Guidelines for Public Health Units (20), and the Australian National Notifiable Diseases Case Definitions (7) streamline the treatment of whooping cough across all States and Territories. These documents ensure that all potential cases of whooping cough are identified as soon as possible, and are treated with the most current and appropriate therapy.</td>
</tr>
<tr>
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<td>Notification of cases to the Public Health Unit – it is a national requirement that both confirmed cases and probable cases are notified to the local Public Health Unit as soon as the treating doctor becomes aware of them (20).</td>
</tr>
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<td>Quarantining of cases and prophylactic erythromycin – the regional Public Health Unit makes decisions on a case-by-case basis regarding the quarantining of young children and older students during pertussis outbreaks, as well as the need for large-scale prophylactic antibiotics, according to the Pertussis National Guidelines for PHUs (20).</td>
</tr>
<tr>
<td>Tertiary (reducing the progress or complications of established disease, including therapeutic and rehabilitation medicine)</td>
<td>Use of correct antibiotic treatment to reduce the incidence of complications in neonates - the use of erythromycin for the treatment of Bordetella pertussis infection in neonates has been shown to increase the risk of infantile hypotrophic pyloric stenosis, QT prolongation and ventricular arrhythmias (21). For this reason, it is essential to use azithromycin as an alternative antibiotic in this age group, as recommended by both the SoNG – Pertussis (18) and the Australian Immunisation Handbook (22).</td>
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years have surpassed the level that could be reasonably anticipated from the cyclical outbreak pattern of past two decades.

Although Australia already has a well-structured, multi-faceted prevention system in place for community protection against pertussis, including freely-available vaccines, financial incentives for both medical practitioners and parents, and guidelines for outbreak management by public health units, more can be done. The new challenges of 2012, including emerging bacterial resistance, growing support for conscientious objection and an increasing adult reservoir, require novel approaches to pertussis prevention.

Together, the Australian Government and the medical profession should focus their efforts on developing a new vaccine, addressing conscientious objection, listing booster injections for adults on the PBS and increasing public awareness about the symptoms of whooping cough.

In this way, parents, doctors and governments can work together to mitigate the growing threat of whooping cough for our youngest Australians.

REFERENCES

In 2012, two students from The Australian National University (ANU) medical school, Simone Huntingford and Phillip Hingley, one lecturer, Ruth Townsend and Dr Lyle Hingley, self-funded a trip to Papua New Guinea (PNG) to walk the Kokoda track. The purpose for walking was to raise money for the Birthing Kit Foundation, an organisation that compiles and distributes birthing kits to women in developing countries. In 1999, PNG became the first country to receive birthing kits. This was in response to the country’s poor maternal and infant health, which is contributed to by a lack of access to antenatal care, skilled birthing attendants, postnatal care and delivering in an ‘unclean’ birthing environment (1). Use of a birthing kit gives women an opportunity to deliver with the use of ‘clean’ equipment which allows for mitigation against infection which might otherwise put mother and baby’s health at risk. The data shows, however, that outcomes are still poor. By way of comparison, the lifetime risk of death for women giving birth in Australia is 1 in every 7400 (2). In PNG it is 1 in every 94 (3). The infant mortality rate in PNG is 47 per 1,000 live births (3), while in Australia it is just 4 per 1,000 live births (2).

We flew into Kokoda and were invited to attend the local Kokoda Hospital where Sister Margaret, the health practitioner in charge, showed us around. The hospital was built by Australian Rotarians and the facilities were basic (4). There is very little government support for health in PNG and the hospital is reliant on generators for electricity. It is relatively well supplied with drugs, but patient meals and linen are supplied by the family. The majority of work undertaken by the small team was to assist women who had developed postnatal complications (most commonly post-partum haemorrhage) and who actually made it to the hospital after delivering in their village. Some villages were hours from the hospital and accessible only by foot across the rugged Owen Stanley Range.

After our initial exposure to the PNG health care system, we set off on our eight day, 96 kilometre trek. On day two, we stopped for lunch at Isurava, the site of four great granite memorial stones marked with the virtues embodied by the soldiers who fought in the Kokoda campaign – mateship, endurance, courage and sacrifice. As we were reflecting on the enormity of the challenge of fighting a war in this difficult terrain, we became aware of a little boy in the village who had a cut finger. With the help of an interpreter, and the trust and openness of the child and his mother, Phil was able to dress the wound. After observing us treat the child, another mother nearby revealed to us a large breast ulcer. Again, we were able to provide care but we had quickly become aware that we had very little medical equipment with us that could provide much more than simple treatment – wound cleaning, simple dressings and antibiotics. Our ability to provide even this level of care was serendipitous. We had ‘over planned’ for what would be necessary for our own care and so we were happy and grateful for the opportunity to give it away to those with a greater need.

As the sun set, we drifted into another village where a gaggle of children sang and danced a greeting for us. We distributed toothbrushes and there were squeals of delight as we took photos of the children to show them what they looked like. They have no mirrors and so this was the first time some had seen themselves. We noticed one of the children had severe impetigo, but were faced with the challenge of delivering a safe and simple paediatric cephalaxin dose given that we were only carrying 500mg capsules. Dr. Hingley knew that the child dose of cephalaxin is 6.25-12.5mg/kg every six hours for five days. After calculating the dosage for the child using an estimation of weight based on his age, we then considered how to develop an easy method of administration. We mixed enough capsules with water in a spare drink bottle for a full course of the antibiotics. We calculated that the child would need 25mL of the solution for each dose. Fortunately, one of the group members had brought along a 30mL plastic ‘shot’ glass and so it was agreed that this would be the most appropriate method.
Whilst tourism has brought enough wealth to those living along the Kokoda track to allow for some villages to have access to a health practitioner, the health care able to be provided was still very limited, and would be even more so the further from the track a person lived. This wasn’t just a problem for those in rural areas. Health care in Port Moresby was equally shocking.

Upon our arrival back in the capital, Simone arranged for us to visit the general hospital. In the labour ward there were no beds for women who had delivered to rest on, and instead they lay on the floor of the ward clutching their newborns. Women who have just delivered are ‘strongly encouraged’ to have a tubal ligation whilst they are in the hospital. This action is justified on the basis that it saves women’s lives. The ward is staffed by junior doctors and overseen by a visiting doctor from New Zealand. There are no midwives. There is no midwifery school. In the paediatric ward there was one nurse. There were one or two units of O-negative blood for the 600 bed hospital. Outdated medicines are used, for example, phenobarbitone was used as first line treatment for paediatric seizures secondary to meningitis. The hospital had little in the way of diagnostic tests including simple genetic testing, and instead, for example, relied only on clinical signs to diagnose conditions such as thalassaemia. PNG is home to one of the largest resources projects in the world, a $30 billion Liquefied Natural Gas (LNG) project, but there is no visible distribution of this wealth to PNG by “enhancing primary care services in village aid posts and rural district health centres” and providing support to experienced clinicians and public health experts to develop the PNG workforce (7). There is little evidence that these recommendations have come to fruition.

The trek was so much more than we had expected it to be. The experience of working with nothing much with those who have nothing much, was profound. It was not only difficult physically and emotionally, but it was a learning experience with exposure to all the components of the medical school curriculum – clinical science, clinical skills, population health, professionalism and leadership. If there were any doubts about the choice to study or practise medicine and the benefits one may give and receive from its practice, then they were answered by this experience. The track compels you to reflect on the great and noble acts performed by our soldiers and the fuzzy wuzzy angels who walked it all those years ago. The practice of medicine offers the hope of making a similarly great and noble contribution, but on our journey, for those moments, we were content and grateful for the opportunity to play our minor part, to relieve some suffering, to make a small difference to the lives of those we treated and to consider what more we can do to help in the future. The journey was at times confronting but enormously rewarding, and we would recommend to anyone that they go and experience it for themselves.

REFERENCES


The need for an emphasis on communication in medical training: if you can’t communicate you can’t be a good doctor

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All efforts to treat a patient are futile if the patient’s concerns are not addressed. Such concerns can only be elicited through communication, which is therefore central to the role of a doctor. Developing communication skills in junior doctors and medical students is not only fundamental to their education, but is proven to protect against adverse medical and legal outcomes. There is no doubt that in more recent years Australian medical schools have made an effort to better prepare students with communication skills. Nevertheless, contemporary research suggests that certain aspects of communication need to be emphasised more in medical school curricula (1,2).

The growing medical profession has positioned doctors in an increasingly complex social and professional network. This has identified the already important need for communication amongst health professionals as central to good practice. A century ago doctors accounted for approximately one in three health care professionals (3). Today, doctors account for approximately one in eight health care workers in Australia and work alongside any number of health care professional including nurses, occupational therapists, psychologists, radiographers, paramedics and physiotherapists to name just a few (4). The growth in speciality vocations within the medical field is further complicated by an explosion in available information. Innumerable journals, websites and textbooks can be found, each applying to different specific professions and often using diverse terminology. Within this changing environment a doctor must integrate information and pass that information onto patients and other staff.

Australia’s society has also changed. Citizens are more health conscious, live longer, have greater access to information and access health care more frequently (5). All these factors contribute to an environment where patients can potentially come to understand their own illness in greater detail and subsequently act independently to rectify them. On the other hand, there is a greater risk of patients being misinformed. In this context there is a strong impetus on the doctor to adequately elicit a patient’s understanding and provide information that is relevant and helpful to them. The informative and communicative nature of the doctor’s role is nothing new as the word doctor itself derives from the Latin verb docēre meaning ‘to teach’.

The central role of communication for a doctor is particularly apparent when considering how much time they spend in communication. A number of Australian studies revealed that communication occupied up to 80 percent of the time that clinicians were observed. Communication in this case was not only defined as face to face conversation, but also conversation through phone calls, pagers and letters (6-8). It is clear that a good doctor needs to be able to effectively communicate through a variety of means. This point is emphasised when we consider the proportion of medical errors attributable to communication problems in Australia and abroad.

Failure in communication has long been cited as a major factor contributing to adverse clinical events in health care. A Californian study showed that poor communication accounted for up to 24 percent of errors in patient-doctor consultations and outpatient surgical centres. Failure to follow-up laboratory results, improper recording of information, and medication dosage mistakes were also important causes of error, all of which involve a communicative element (9). In the United Kingdom, the National Confidential Enquiry into Perioperative Deaths showed that shortcomings in teamwork and communication were a central contributor to the lack of improvement in the number of patients in England and Wales who died within three days of surgical intervention (10). An Australian report suggested that 15% of all human error was attributable to communication problems (11). Indeed, the Harvard Medical Practice Study (12) and the Quality in Australian Health Care Study (13) have both exposed ineffective communication as a significant contributor to medical error. Communication failure has also been identified as a major precipitant of litigation.

Mistakes are inevitable in medical practice, but this does not necessarily lead to litigation. A 15 year study revealed that doctors who ignore the importance of good communication with their patients are more likely to be sued (14). The likelihood of litigation has also been shown to be highly associated with feelings that the doctor has covered up facts, has not provided the information requested, has not listened to the patient, or has deliberately misled the patient (15). All these factors are intrinsically related to how a doctor communicates with the patient.

Very subtle communicative features have been shown to influence litigation. For example, an analysis of 114 conversations between 57 orthopaedic and general surgeons with their patients showed that surgeons who sounded less concerned and more dominating were more likely than other surgeons to have been sued (16). Developing very specific and subtle communication skills is of great importance to any medical student who wants to avoid making their future mistakes worse through precipitating litigation. Furthermore, communication is critical in allowing informed consent from the patient.
In many respects, informed consent remains the single most important issue in the delivery of health care. If a procedure is carried out without informed consent, the doctor (or relevant agent) is guilty by law of assault and in breach of the essential ethical obligation to respect the autonomy and inherent dignity of a patient. Ultimately, the patient must be granted the decision of what treatment is best for them. To do so, they require clear information on the nature and purpose of any intended investigation or procedure, the available options, the pros and cons of each option, what the treatment involves, side effects, possible complications, and what to expect both during and after the treatment. Obviously it is difficult to communicate all these ideas well, leaving patients with little power to make their own decisions. Several studies have demonstrated that patients in fact retain little of the information given to them during any consultation (17). The presentation of information to patients is clearly vital in the communication process and even with the numerous multimedia resources available within Australia, patients commonly report being uninformed and unsure on where to find information regarding their condition (15). This is of utmost concern in respect to the patient’s ability to give informed consent and also draws attention to another aspect of communication that needs to be worked on in medical training.

Medical schools in Australia have recognised the critical need for better teaching in communication skills. In comparison to earlier programs, current medical school curricula better addresses communication skills through various initiatives such as increased patient contact, simulated interviews and community health placements (1,2). Nevertheless, as revealed by the Australian Medical Education Study (AMES), more needs to be done to fully develop communication skills in medical school undergraduates.

In 2007, the AMES revealed that undergraduate preparation for difficult communication situations was thought to be poor amongst students and health care workers, and communication within, or understanding of, the clinical hierarchy needed to be better addressed in medical schools across the country. More positively, the report concluded that general communication skills for patient-doctor consultation scenarios were thought to be well covered by the medical schools amongst both students and physicians.

The findings from the AMES suggest that communication situations outside the typical consult scenario need to be addressed in Australian medical schools, particularly interprofessional communication (1). To a certain extent, more emphasis is being placed on interprofessional communication within medical schools. For example, initiatives such as Interprofessional Learning (IPL) seminars are taking place in many Australian Universities including The Australian National University and The University of South Australia. Nevertheless, as the AMES report would suggest, these schemes have not sufficed in silencing critics of Australian medical school curricula more generally.

From my own experience in medical school, I believe that some more formal and explicit training in conflict control and working in groups would be of great benefit to undergraduate medical students and complement the various IPL initiatives well. Other communication areas that may benefit from further attention in medical school curricula include how to communicate complicated pathophysiology to naïve patients and script writing. In my view, these areas are crucial to the practice of the doctor but are often not formally addressed in medical teaching.

The practice of medicine is more than the application of tests, diagnoses and treatments. It is based on a relationship between practitioner and patient and as such encompasses the art of human interaction. The essential need to constantly develop communication skills in medical practitioners both in Australia and abroad must not be forgotten. Developing effective communication among doctors is an ethical obligation to the patients and clearly important in reducing the occurrence of adverse medical outcomes as well as litigation in the medical profession. The need for Australian medical schools to continue to emphasise communication training should not be underestimated. It is important that students and teachers alike continue to think about how the various communicative skills in medical care can be taught well.

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Osteoporosis has historically been considered a woman’s disease and has not received the same degree of awareness in men. About 50% of women and 25% of men will have an osteoporosis-related fracture in their lifetime, resulting in significant morbidity and mortality (1, 2). Even though roughly 1 in 3 osteoporosis-related fractures occur in men, this disease remains under-diagnosed and under-treated.

**CASE STUDY**

“Mary”, an 82 year old female, and “John”, an 80 year old male, seen in different general practice settings, both underwent rehabilitation for similar pelvic fractures after falls at home. Mary had a bone density scan and was diagnosed with osteoporosis. She was then given information on osteoporosis, future fall prevention and prescribed a bisphosphonate, calcium and vitamin D supplements. John had two previous fractures and a smoking history but was not investigated for osteoporosis and received no information about osteoporosis treatment or prevention.

**BURDEN OF DISEASE**

Osteoporosis and its related fractures represent a major public health issue. Worldwide there are approximately nine million new osteoporotic fractures a year, contributing to chronic pain and disability, as well as morbidity, mortality, institutionalisation and economic costs (3). An Australian study revealed that the lifetime risk of an osteoporotic fracture in women over 50 years is 43% (increasing to 56% in women over 60 years), while the lifetime risk is lower in males over 50 years at 27% (increasing to 29% in males over 60 years) (4). However, this risk in men is still much greater than many other chronic conditions.

Of all osteoporotic fractures, hip fractures contribute most of the burden in terms of morbidity and mortality. Interestingly, in males the mortality after a hip fracture is two to four fold higher than in women (5, 6). The exact reasons for this are unclear, but it is worth considering that inadequate management of these males could play a role.

**DIAGNOSIS**

Diagnostic assessment for osteoporosis should include a medical history, clinical examination, and dual-energy X-ray absorptiometry (DEXA) bone density measurements of the antero-posterior spine and hip. According to Medicare Australia, the bone density measurement testing rates are four times higher in women than in men (7). This low rate of testing in males suggests that a diagnosis is not typically made until after a fracture has occurred and the associated morbidity is already present.

The Royal Australian College of General Practitioners (RACGP) states that “there is good evidence to support general practitioners investigating any individual with risk factors for osteoporosis” (8). The main risk factors include low bone mineral density, past history of fracture, age (>70 years), gender and multiple falls, with further risk factors including smoking, immobility and high Body Mass Index (BMI). Additionally, it has been found that 50% of men who have an osteoporotic fracture have identifiable risk factors for secondary osteoporosis (2). These include hypo-gonadism, glucocorticoid therapy, gastrointestinal disease, Vitamin D deficiency, anti-convulsant drug therapy, hypercalciuria, and alcohol abuse (2). This suggests there are many men in the community with risk factors that should alert their general practitioner to investigate for possible osteoporosis.

Patients who have had a prior osteoporotic fracture are at higher risk for future fractures (9). Accordingly, the RACGP recommends that general practitioners investigate all patients with minimal trauma fractures (8).

**PREVENTION**

There are many known modifiable risk factors for osteoporosis including low Vitamin D, low calcium intake, lack of physical activity (in particular weight bearing exercise), smoking and excessive alcohol intake. These risk factors should be discussed with all patients, and in particular, those with risk factors for osteoporosis that were previously mentioned. In addition, strength building exercises and falls prevention are important to reduce the morbidity and mortality associated with an osteoporotic fall.

Pharmacological management includes bisphosphonates, hormone therapy and strontium ranelate for certain patients. Unsurprisingly, it has been found that males are less likely to receive anti-resorptive therapy after a hip fracture (4.5 versus 49.5%, respectively) (10). Unfortunately, this is likely to contribute to poorer outcomes if another fracture was to occur.

In summary, both male and female patients should be investigated and managed for osteoporosis as recommended by the RACGP guidelines, to help prevent mortality and reduce the large burden of chronic pain and disability.
REFERENCES

The sexual history is a vital part of a number of medical disciplines, ranging from infectious diseases to urology, obstetrics and gynaecology, general practice and psychiatry. Yet despite its importance in both the diagnostic and management components of medicine and surgery, the sexual history is often forgotten or glossed over. What is it about the sexual history that deters us from delving into this important area of our patient’s presentation?

In an article published this year, Sobecki et al. reported that amongst a cohort of American obstetrician/gynaecologists, 63% routinely assessed patients’ sexual activities, 40% regularly asked about sexual problems, 28.5% asked about sexual satisfaction, 27.7% learnt the patient’s sexual orientation/identity and only 13.8% evaluated the patient’s pleasure with sexual activity (1). This study demonstrated that while many obstetrician/gynaecologists may inquire about sexual practice, many do not sufficiently explore the matter. Even in a field deeply engaged with patient’s sexuality, it is shocking to consider that the sexual history is so often forgotten.

In Australia, few studies have examined the pervasiveness of sexual history taking in health care settings, though the available evidence suggests that a similar phenomenon exists. In a 2008 study, Khan et al. demonstrated that amongst 409 general practitioners, 69% felt comfortable discussing sexual health and managing sexually transmitted infections (STIs) in heterosexual or young patients, while only 40% felt comfortable having the same discussion and managing the same pathologies in patients who were gay, lesbian, intravenous drug users, indigenous or sex workers. Practitioner discomfort in the domain of sexual health was strongly associated in this study with limited or incorrect sexual history taking, suggesting that many health providers lacked the skills or confidence necessary to approach this important topic (2).

Indeed, one of the key reasons that the sexual history is often avoided is that many physicians lack a comprehensive system to guide their discussion with patients. In order to encourage health professionals to engage in this element of the patient’s presentation, the American Center for Disease Control and Prevention (CDC) has outlined the “5 Ps” of the sexual history: partners, practices, protection from STIs, past history of STIs and prevention of pregnancy (3).

When discussing partners, it is vital to establish the sex of the patient’s partners (male, female or both), to ascertain the number of partners (in the last three months and the last 12 months) and to establish the relationship between the patient and his/her partner(s) (monogamous, multiple casual, multiple regular). It is also vital to ask about sexual intercourse with sex workers or with partners met on the internet, as both of these are risk factors for STIs.

When inquiring about practices, establish the type of intercourse performed (oral-genital, oral-anal, anal-genital, vaginal-genital, anal-digital, vaginal-digital), whether or not the patient engages in diverse sexual practices (e.g. violent sex) and whether the patient has experienced any harmful or non-consensual sexual encounters.

To assess protection from STIs, inquire about barrier contraception methods (e.g. condoms) and STI prevention practices. Confirm whether the patient has had any pertinent vaccinations (such as those against Human Papilloma Virus, Hepatitis A Virus, and Hepatitis B Virus) and whether the patient feels comfortable and confident in his/her current STI prevention strategy. It may be prudent to ask about classical signs and symptoms of STIs, including discharge, pruritus, erythema or other skin changes, pain or systemic symptoms.

Evaluating past STIs includes establishing past diagnoses (with discussion of symptomatology), methods of detection, treatment regimens and any complications experienced. Such questioning should also be asked about the patient’s partners’ past STI history. Use of post-exposure prophylaxis should also be assessed. Ideally, an open discussion with the patient about his/her experience of previous STIs, in particular, with contract tracing, follow-up and compliance should follow.

Prevention of pregnancy should cover the gravity and parity of the patient or his/her partner where relevant, the use and type of contraception (barrier methods, hormonal methods, devices and/or practices) and any adverse effects from the contraception method. It is important to specifically inquire about the use of emergency contraception (the “morning after pill” or high dose progesterone). The personal importance of pregnancy prevention should be ascertained from the patient.

Before ending the sexual history, it is also vital to assess for Human Immunodeficiency Virus (HIV) and hepatitis risk. Though most of the elements of the patient’s salient sexual history findings should have already been gathered, it may be important to ask about current or past sexual intercourse with individuals from high risk countries or with individuals with known HIV. A history
of injecting drug use of the individual and his/her partners is also vital. Previous vaccinations and blood tests should be clarified if they have not been previously.

Throughout the history taking process, it is vital that the physician remain non-judgmental (4). This involves both verbal and non-verbal elements, and students should be aware of the enormous influence that facial gestures can have on a patient’s willingness to discuss the issue of sexuality. It is also vital that physicians approach the sexual history with confidence – being comfortable and relaxed in the history taking process will allow for a more honest and informative discussion, and will let the patient know that you are genuinely interested in what they have to disclose.

The sexual history is often forgotten or, if approached, rushed through. This is to the detriment of any physician working through the often complex array of symptomatology related to the sexual practices of a patient. Indeed, the sexual history provides an enormous wealth of information to the physician, allowing him/her to gain a deeper understanding of the patient in question.

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Ghana – an unforgettable elective experience

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Ghana is a beautiful, diverse, welcoming and unforgettable nation and it is for these reasons, and many others, that I am thrilled to have had the privilege of completing my medical elective there in January 2012. I organised my elective through International Volunteer Headquarters (IVHQ), a New Zealand-based company that offers volunteer experiences in a number of developing countries around the world. Upon my arrival in Accra (the capital of Ghana), I was greeted by a local representative and brought to the volunteer house where I had orientation with all the other new volunteers, following which we were sent off to our various locations. I was heading to a tiny town in the Eastern region of Ghana called Frankadua.

The Frankadua Health Centre is a small medical centre servicing the town of Frankadua and the surrounding Asogyaman region (total population ~4000 people). It is operational 24 hours a day, 7 days a week and the staff residence is located behind the clinic so someone is always on hand if needed. The clinic is run entirely by nurses and midwives. Nurses who have just completed their training through the Ghana Health Service can be allocated to a clinic anywhere in the country where they must work for a minimum of two years. While the standard of the facilities and the resources available was surprisingly good for rural Africa, it is still very much behind the luxury of what we experience here in the Western world. The focus of the clinic was on general practice, with a particular interest in women’s and children’s health. Antenatal consultations were commonplace and the clinic additionally functioned as a labour ward. Many of the pregnant women who presented were under twenty years of age and had no understanding of contraceptives or family planning. An important part of each of these antenatal consultations was explaining the concept of safe sex both in regards to the chances of falling pregnant and the risk of acquiring a sexually transmitted infection.

Baby check and immunisation clinics were held in the neighbouring villages of Fintey and Abodemoyo monthly and were very well attended by the local women and children. The method of weighing the babies was quite amusing – they were placed in what looked like calico shopping bags with holes for the legs and were hung from the scale. The national immunisation schedule included vaccinating children against measles, mumps, rubella, streptococcal pneumonia, chickenpox, polio, diphtheria and tetanus, as well as receiving vitamin A.

The staff rarely examined patients, generally relying on history alone to form a diagnosis and management plan. Antenatal presentations were the only consultations in which any physical examination took place. The midwives would measure the fundal height and listen for the foetal heartbeat by pressing their ear to a fetal stethoscope, a wooden trumpet-like instrument placed on the mother’s abdomen. I found it quite interesting that they did not have any ordinary stethoscopes, however they had an automatic blood pressure machine.

The method of diagnosing patients was also interesting to observe. The staff appeared to have a list of ten or so diagnoses that all patients fit into. These included gastroenteritis, chest infection, skin infection and urinary tract infection. Additionally, the majority of patients were treated for malaria, regardless of whether their symptoms suggested it or the on-the-spot testing was positive or negative. Each patient left with some kind of medication, the majority being antibiotics and ibuprofen. The medications are provided for free by the Ghanaian government as part of the National Health Insurance Scheme.

While the Frankadua Health Centre functions predominantly as an outpatient facility, the centre has an ‘inpatient’ area consisting of four beds. Patients could be treated with IV fluids here and new mothers were welcome to stay with their babies after giving birth. The sicker patients were sent to Akosombo Hospital, which is just over an hour from Frankadua. Often patients had to travel to the hospital via tro-tro (tightly packed, poorly serviced minibuses which act similarly to a bus service), although there are a few local residents with vehicles who can provide an ‘ambulance’
service if urgently required.

My brief lesson in the language of Twi did not prove to be of any benefit where I was located as the people in Frankadua (and the majority of those in Volta region) speak Ewe, which is also the national language spoken by the people in the bordering country of Togo. By the end of my placement, however, I was able to speak some words in the local tongue which both impressed and amused my newfound friends. The language barrier was quite a challenge at times working in the clinic, and this meant that one of the other staff members needed to be a translator for me quite frequently. I found this to be quite frustrating and at times felt that my presence was a hindrance rather than a help as each consultation took that little bit longer.

Medically, my experience was not exactly as I had expected. While I did get a sense of the common presentations in rural Ghana and was able to gain an appreciation of how family planning and antenatal care is handled, I think I would have got more out of the experience had my time been shared between the clinic and the nearest hospital. This would have allowed me more hands-on experience and I would have preferred to spend some time with the physicians working at the hospital.

Culturally, my experience was unbelievable. As a single female sometimes travelling alone I did not encounter any problems or have any serious concerns for my safety. I was, however, proposed to on multiple occasions which did wonders for my self-esteem! I lived in a small room within a complex that also housed local villagers, and thus was essentially living in a homestay. There is honestly no better way to fully immerse yourself in the culture of a country than to live right where the action is. Be warned, however, that modern luxuries are not present in rural locations such as Frankadua. We had no running water (cold bucket showers were the go) and sporadic electricity but I think that’s all part of the fun. I spent my mornings assisting at the clinic and my afternoons chatting to the locals and playing with endlessly energetic kids. Football (or soccer to us Aussies) is popular and despite my limited knowledge of the sport, I found myself watching Ghana play in the African Cup of Nations with bated breath. Whenever Ghana scored a goal the excitement was intoxicating and I couldn’t help but cheer and dance with the locals. The weather was beautiful for my entire stay (I was visiting in the dry season) and the sun did not set until late in the evening. As part of the program, all meals were prepared for us by one of the local residents. She was an amazing cook and I thoroughly enjoyed sampling traditional Ghanaian foods, my favourite being groundnut soup and rice balls. Be prepared to live on a very carbohydrate-rich diet, as fruit and vegetables were sometimes hard to come by. Water was also provided, but not in bottles, rather in plastic bags which took some getting used to before I could open them without spilling water all over myself!

Although I journeyed to Ghana on my own, I easily made friends with other volunteers which made travelling around the country on weekends easier and more enjoyable. The country itself is fantastic and diverse and I highly recommend seeing as much as you can. For me, more often than not, my travels ended up being more about the journey than the destination. I spent weekends at Cape Coast with beautiful white sandy beaches and historical forts, climbing mountains and waterfalls in the Volta region, went on crazy endless bus rides to Mole National Park in the scorching northern region for savannah and water safaris, explored mosques and castles in Wa and Tamale and even had a drink with a chief!

I would highly recommend venturing to Ghana to complete your elective, and even organising it through IVHQ (the cost for four weeks is very cheap) although flights are expensive. Medically, it would be best to try and orchestrate a program whereby you get to work both in a local village medical clinic and at a larger hospital.

Wherever you choose to go, remember that your elective is what you make it!
Ten simple rules for your North American elective

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Australia has become an increasingly attractive place for North Americans to receive their undergraduate medical degree. Many factors, including the quality of education, are responsible for the increase in numbers. An elective experience in North America is essential for students planning to return home to practice medicine. Practical experience familiarises students with the health care system and provides an opportunity to acquire references for postgraduate training ('residency') program applications. Developed from our own experience, the following article highlights ten important aspects that medical students should consider when arranging and attending their electives in North America.

1. CHOOSE THE RIGHT ELECTIVE

The elective is your opportunity to demonstrate your work ethic, attitude and ability. If you know what residency program you are going to apply to, choose electives related to this field. If you are unsure, choose more general specialties. Ideally, electives will be organised through institutions that are involved with postgraduate training. Electives are a personalised experience with professional ramifications. Given limited elective time, balancing factors like visiting prospective residency locations and returning to your hometown are important. Choose the right elective for you.

2. SUBMIT YOUR APPLICATION EARLY

The process of applying for an elective in North America is becoming increasingly competitive every year. Each university has a unique application process, so do your research ahead of time and learn about deadlines and requirements. Your university provides information on malpractice insurance and ensures the elective fulfills your school’s requirements. Submit your complete application package as soon as allowed, which may vary from six to nine months in advance. Expect, and even anticipate delays, the process is always slower than you expect.

3. LEARN THE SYSTEM YOU ARE IN

Medicine has common basic standards, yet each hospital, and seemingly every specialty, will have a different approach. In North America the clinical years, referred to as the clerkship, essentially integrates the Australian clinical years and internship. Students learn by taking on an active role. Being treated as junior members of the team engenders increased responsibility. Importantly, there is an increased focus on management that you may not have experienced in Australia prior to your electives. Asking for help early on can solve challenges arising from the subtleties in different protocols. Do not force old routines, adapt to your new surroundings.

4. LEARN FROM EVERY OPPORTUNITY

Clerking a patient in North America is time-consuming and tiring, yet a very rewarding way to learn competent clinical care. Local students are often required to work many hours, including weekends and overnight on-call shifts. Elective students should actively pursue the opportunity to do the same. Immersing yourself in the role provides you with a better idea of the culture of the program, and how well it fits with your training style. Consider everything a learning opportunity, even the tedious moments. Your keenness will make you stand out.

5. LET THEM KNOW YOU WANT A REFERENCE

Good reference letters are an essential component of a good residency application. Inform your preceptors that you want a reference. It is okay to ask at the end of the elective, however asking early allows your preceptors to be more conscious of it. Take the opportunity to talk about your future interests and goals. Some students ask their preceptor to prepare a reference document during or shortly after the rotation, since references are often not required immediately, and specific details may be forgotten.

6. FIND A USEFUL ECTOPIC BRAIN

No clinician will remember everything about medicine. It is important to know where to look. Traditionally, a small notebook is carried that includes the essential components for clinical practice. However, smart phones are an increasingly common and simple way to stay informed. Investing in good applications will provide key tools for managing simple ward-call problems and prescribing different medications. If you are unsure which to use, ask your colleagues for suggestions.

7. MAKE FRIENDS

Be friendly with all professionals you come into contact with. Nurses and allied health practitioners are essential to ensure your patients receive excellent care. They can also be valuable resources. Other medical students, especially those familiar with the system, can help to ensure you get the most out of your experience. Further, students mostly spend time with residents or fellows. These doctors teach you the day-to-day skills and provide
feedback to the consultants who write your letter of reference. Any physician or resident could be a member of the selection committee.

8. MEET WITH THE RIGHT PEOPLE

Electives are your opportunity to meet with various staff and program directors. Your elective does not have to be with the head of the department, but take the time to meet with him or her. Find out more about the program and the application process, express your interests and intentions, and provide a face for application reviewers to remember.

9. WORK HARD

Expect to work hard when on elective. Consider your clinical experience an extended interview. In the North American system, final year medical students are considered junior members of the team. Show up early. Leave after the work is done. Be polite and enthusiastic. Smile. It is okay to not know the answer, but do your homework. Never answer the same question wrong twice. Take advantage of the opportunity to demonstrate your willingness to learn. Volunteer to help. Do extra reading and research on your cases. The impression you leave becomes a part of your residency applications.

10. ENJOY YOUR TIME OUTSIDE THE HOSPITAL

North American electives are very important for your residency application, but always remember to enjoy the time outside of the hospital. It can make those long days and nights more worthwhile. Finding a location you would feel comfortable calling ‘home’ is an important part of the process. The best applicant is skilled, enjoyable to work with and integrates well into the community.

CONCLUSION

North American medical electives are an essential component of a strong post-graduate training application. These ten simple steps provide a framework to maximise your elective experience. Specific details for ensuring a smooth process will vary. Start early and be prepared. When in doubt, ask those who have already done a similar elective. They are usually more than happy to assist. Enjoy your clinical training and be sure to pass on any wisdom to those who follow.
An elective experience in rural and remote Uganda

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After a three hour journey from Kampala fellow medical student, Alan, and I reached the turn off point for Ibulanku – a small rural community in the Iganga district of Uganda. Here the road turns from bitumen dusted with potholes to dirt. Only the occasional motorbike passes us, cars are rarely seen and people are mainly walking or otherwise on pushbikes. Kids are out in ragged T-shirts waving and happy to see us, shouting “mzungus!” (“white people”). We passed several games of soccer, women and children carrying water from the bore holes or babies slung across their backs. Small mud brick houses scatter the roadside, surrounded by small patches of subsistence farming.

We arrived at Ibulanku at around 4pm in the afternoon at the end of December – a particularly hot and sticky day. In front of the house was mould of corn left in the sun to dry, with the odd goat or chicken wandering amongst it. The manager of the clinic left us with our bags to settle in. We both sat for a while on the chairs in what was a luxurious mansion compared to what most locals lived in. After all it had flushing toilets, running (cold) water, and mosquito nets. We noticed a sign on the wall inside the living room that we found intriguing: “Rules of the house – no children allowed inside. Also, keep them away from the windows”.

We were both taking in everything that had happened throughout the day as well as what we had seen of the village. We had just met ‘Grandma’ who lived in a mud brick house attached to ours - apparently she was to do our washing. We then met one of Grandma’s orphans – 11 year old Raymond - who soon became our interpreter and would often shoo away other curious children from our house. As the sun set we started to make dinner when the power went off. This was to be a regular occurrence in Ibulanku as it was in other areas of Uganda - not enough power for everyone means that it is rationed throughout the country. Sometimes we went without power for days. While many people lived without power, it did become problematic for hospitals to always rely on expensive generators. So, as we cooked the first of many meals by candlelight we understood why the aforementioned sign was posted – children from the village soon swarmed the windows of our house laughing and yelling “Mzungus! Jambo Mzungus!” The same phrase was always heard many times on our daily jogs in the village along with “How are you?” which was usually followed by “I’m fine!”

Our first day in the clinic consisted of a ‘tour’ of the Ibulanku health centre next to the house where we stayed. We were shown around the hospital and introduced to many welcoming staff – midwives, nurses, a laboratory technician as well as the clinical officer, Nathan – more than a nurse but not quite a doctor. The facility was basic with two paediatric wards, a women’s ward and a men’s ward, as well as a maternity unit (probably 30-40 beds in total). There was a small room for analysing various samples – the great majority of which was blood smears looking for Plasmodium falciparum (problematic when the power was out and the sun was down). The tour of the hospital quickly turned into a ward round where we were asked to examine patients and give our opinion on diagnosis and management. I think we saw about 12 patients that morning, all of whom had malaria of which we really knew very little about. While examining one patient who was particularly ill with malaria, I have the distinct memory of a mosquito humming around, attempting to land on my arms as I subtly tried to wave it off.

Later that day we then took a tour of the annex facility in neighbouring town Iddi. This facility was in a town centre, unlike Ibulanku, which was in a village. Although in the town centre, there were still cows and goats that would wander the street out the front. The busy centre had about five small rooms out the back that were crammed with patients, most receiving IV fluids and quinine for malaria. This centre was staffed mainly by nurses who worked incredibly hard and did a great job given the volume of work and the limited resources available.

Our days onwards consisted of rotating between the two health facilities, usually with the morning at Ibulanku and the afternoon at Iddi. Transport between the two centres was via a “border-
border”, i.e. a motorbike with three of us on the back of it, the third being Budhima - another ANU student who arrived shortly after us.

At Idudi we soon began to get a reputation as the ‘white doctors’ who could cure and many elderly people came to see us. It was quite challenging at times to have all these patients (who usually didn’t know their age), come with multiple health problems. Many patients couldn’t afford to go to a larger hospital as they couldn’t afford the bus fare or couldn’t afford the treatment. For the people that we were seeing in the villages, we were told the average wage was about 300,000 Ugandan Shillings a year (roughly equal to $100 Australian). While some health care was free, the cost of any investigations generally came out of the patient’s pocket and so did the cost of medications. Some medications for TB, malaria and HIV were free, funded by the Australian and US governments. However even a urine dipstick cost roughly $1 AUS, and patients at the Ibulanku centre would pay for any IV fluids as well as the cost of the giving set, cannula and other drugs.

Ibulanku health centre also ran outstation visits, where a group of health workers along with a group of volunteers would travel to a smaller village within the district and educate the people on malaria, HIV, vaccinations, as well as nutrition and health during pregnancy. These were a fantastic part of the clinic’s work and great to attend. The volunteer drama group performed and danced with traditional music – everyone could see that it was a fantastic educational message especially to the children who loved the entertainment.

During our time in Ibulanku we also attended the HIV clinic where many people were seen and usually given co-trimoxazole to last them for the month. The memory I will always retain from this is one where a ten year old girl with such a look of sadness and shame came in on her own to collect her medication, having been orphaned at a young age as her parents had HIV. It reminded me of fact that in Uganda, unlike Australia, so many children are burdened at far too young with not only the responsibilities of adulthood but also by diseases that are preventable.

One Sunday in Ibulanku we attended the local “happy clappers” church which was an unforgettable experience – lots of singing, dancing and chanting over several hours. We were warmly welcomed to the group and fellow medical student Budhima was invited to read from the Bible and be personally anointed by the Pastor in front of the congregation. The Pastor’s energy was truly a site to be seen.

After four weeks on our placement in Ibulanku we all left feeling like we had achieved something for ourselves – we had learnt a lot about diseases that are rarely seen in Australia, had seen patients on our own, and attempted diagnoses based on clinical suspicion alone (all through the work of translators i.e. the nursing staff). Above all we had met so many wonderful people who had so little compared to us but who still did so much for their people and community and did it with a carefree smile. On our last night in Ibulanku, the staff put on a BBQ for us that included dancing and singing. We were also given traditional African outfits to wear for the night and to take home with us.

And now, in my comfortable house in Canberra with the heater on and a cup of tea, I’m reflecting warmly about my time in Uganda, and I can see all the faces of the people and children that we met. These happy images remind me of how much I loved Africa and how much I’d like to return. But at the same time I reflect with a sense of overwhelming sadness as I think about all the health problems and poverty in the country. I think of the corruption and inequalities that are so engrained in the culture. I think about the overworked staff and the enormous demand for health care. I think about how the outstation visits that Ibulanku ran were just touching the need for health education. And lastly I think of how incredibly fortunate we are to be in Australia, with such easy access to health care and all its basic requirements.
Man-flu: is it real and why could it be?

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Many men are familiar with being mocked for their tendency to revert to childhood as they suffer the symptoms associated with the common cold. On the other hand, women seem to plough on oblivious to the suffering associated with the renowned rhinoviruses. This disparity in symptomatology is now commonly known as the phenomenon of ‘man flu’. Recently, much to the delight of men, some scientific basis for the man flu has been authenticated.

A 2010 study from the University of Queensland revealed that pre-menopausal women may have a stronger adaptive immune response to rhinovirus infection than men (1). In the study, blood mononuclear cells were isolated from 63 healthy individuals and grouped by sex and age (≤50 years old and ≥52 years). These cells were then cultured with rhinovirus in vitro. Various cytokines produced by the mononuclear cells were measured at different times (24 hours and 5 days) to indicate the extent of adaptive and innate immune responses in each cell sample. The results of the study showed significantly increased levels of adaptive cytokines (Interferon-γ (IFNγ) and Interleukin-13 (IL-13)) produced by cells of women under the age of 50 years (p < 0.02 and p < 0.05 for IFNγ and IL-13 respectively) and women over the age of 52 years (p < 0.02 and p < 0.01 respectively) compared to age matched men. Contrarily, no differences between sexes in the expression of the innate immune system chemokine interferon-gamma-inducible protein 10 (IP-10) were found (p>0.05). As the authors of the study imply, these results are suggestive of differences in the adaptive immune response to rhinoviruses between men and women.

It is interesting to note that given the high prevalence of rhinoviruses in the community, little literature exists on whether immune responses vary in relation to sex (1, 2). With more studies like that described above, further attention is being given to the variance in presentation of common viruses between age and sex. Further research in this area may be useful in promoting a better understanding amongst clinicians in primary care settings of how symptom profiles can vary between gender and age. At this point, however, with the limited scope of research available it seems that men’s inability to get out of bed when they have a cold may well be a legitimate explanation. For the men who suffer from man flu this has some benefit.

Regardless of the usefulness in understanding how the cold may present differently between the sexes, the question as to how something like the ‘man-flu’ could come about undoubtedly has some interesting (and possibly sexist) potential answers. A number of evolutionary theories have been proposed. One such theory from a study at the University of Cambridge suggests that men’s proposed lower adaptive immunity may have paradoxically resulted from a greater exposure to infectious pathogens (3). Explained very crudely, the theory suggests that through greater risk behaviour over time, men have had a greater exposure to infectious agents. To protect against developing prolific adaptive immune responses (i.e. autoimmune conditions), they have evolved lower immunocompetence than females.

Obviously there is more to be said about the topic of man-flu. More recently the topic has received some attention within the media and in academic journals. Unfortunately, a full discussion of the topic is beyond the scope of this article. Nevertheless I found a little reading proved its worth for interesting and robust conversations and would welcome MSJA readers’ input.

REFERENCES
