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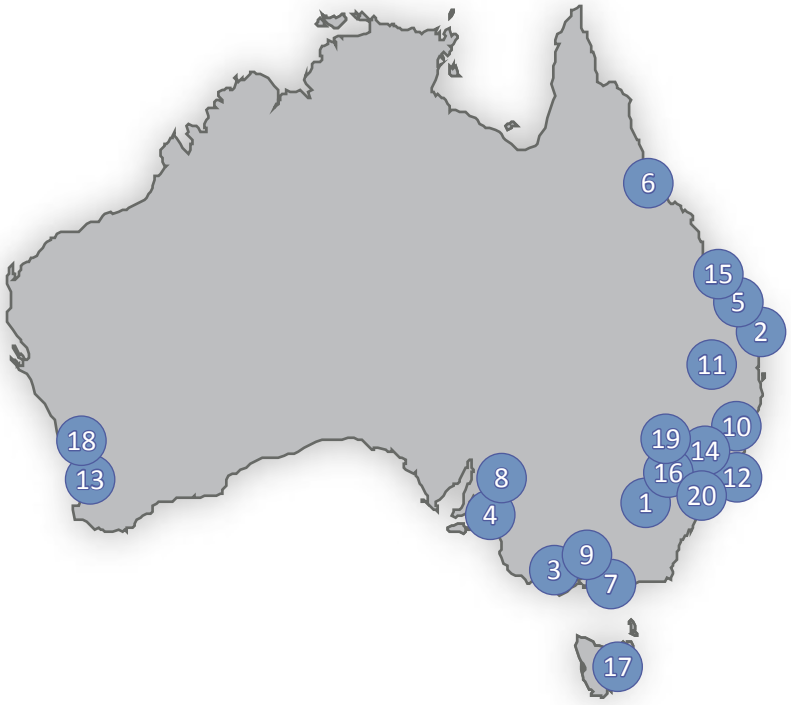
Contents



1. Australian National University
2. Bond University
3. Deakin University
4. Flinders University
5. Griffith University
6. James Cook University
7. Monash University
8. University of Adelaide
9. University of Melbourne
10. University of Newcastle
11. University of New England
12. University of New South Wales
13. University of Notre Dame (Fremantle)
14. University of Notre Dame (Sydney)
15. University of Queensland
16. University of Sydney
17. University of Tasmania
18. University of Western Australia
19. University of Western Sydney
20. University of Wollongong

Crossing boundaries - the expansion of the AMSJ

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Alexander Murphy
External Director, AMSJ

Praveen Indraratna
Editor-in-Chief, AMSJ

From treating acute blood loss in children to palliative care barriers for the elderly, this issue truly showcases the enormous potential and diverse interests of Australian medical students. Our authors have not been afraid to address controversial issues such as emergency department waiting times, healthcare financing and comparisons between barrier exams across Australian medical universities. We are also privileged to be sharing the insights of four remarkable professorial guest authors. Former Australian of the Year recipients Fiona Stanley and Ian Frazer shed light on future directions of research; the IVF and stem cell research pioneer Alan Trounson reflects on progress in his field and Alden Harken, Professor of Surgery at the University of California San Francisco reminds us how fortunate we are to be in medicine.

A core focus of the AMSJ is to become a national journal, that is, one which represents fairly and equally the academic and research achievements of students Australia-wide, without ties to a particular university. The journal has expanded widely in recent months, our current editorial team now spans four states, and we are moving towards full nationalisation of our staff for future issues. Meeting our readers is also a key priority in shaping a national journal, and we were very pleased to hear many positive comments and suggestions from those who attended the AMSA National Convention and Global Health Conference in July.

One of our exciting new initiatives is the AMSJ Blog, updated regularly at our website: www.amsj.org/blog. Authored by staff members, it provides personal perspectives on medical student life, with articles ranging from practical educational posts to lessons learnt outside the hospital, and tackling the bigger questions we all ask ourselves from time to time ('So you don't want to be a doctor anymore?'). We hope you take a look at this terrific new forum for student participation.

As always, support for the AMSJ across Australia's medical schools has been extraordinary, with the free print copies being in huge demand. Remember that you can download the entire journal for free from our website. Articles from the AMSJ will soon be available on the EBSCOhost database and have gained interest from other major academic research databases and indexing systems. We have also had the pleasant 'problem' of reaching our friend limit on Facebook and are switching to a new AMSJ Facebook page: www.facebook.com/amsj.org so please make sure you visit and click 'Like' to stay up-to-date!

The journal is a massive undertaking, and we are grateful to have a wonderful and dedicated volunteer staff of medical students and peer-reviewers who work very hard to make this journal a success. Of course we also thank you, our readers, for welcoming and supporting us as the AMSJ continues to display the research abilities of Australia's medical students.

Some staff of the AMSJ. Clockwise from left: Patrick Teo, Timothy Yang, Matthew Schiller, Chris Mulligan, Praveen Indraratna, Aaron Tan, Alexander Murphy, Grace Leo, Veronica Lim and Helena Jang.

The great wall of medical school: A comparison of barrier examinations across Australian medical schools

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From the moment that a medical student receives their university offer until the moment they take the Hippocratic Oath in front of proud family and friends, they will tread a path only taken by a select number before them. However, with medical schools now in every state and territory of Australia, the journey will not be identical for all students. For some, this will be a marathon, with continuous assessment peppering the entire journey, while others will encounter multiple large hurdles, interspaced with periods of calm. Despite this very different experience of medical school, all will ultimately compete for an increasingly competitive pool of internship positions, which represent the key to unlocking their future medical careers.

The 'Barrier Examination' is a common term used for the final set of assessment of a medical student before being allowed to graduate as a doctor. At most medical schools, this is held in the final or penultimate year of study, and often consists of a combination of written (such as Multiple Choice Questions – MCQ) and clinical assessment (i.e. Viva Voce and Observed Structured Clinical Assessment – OSCE). It is known that barrier examination formats vary widely between medical schools, which raises a number of questions: which examination format is the most accurate at predicting future clinical performance? Which format is most accurate at assessing knowledge and skills? And can students from different universities ever be accurately compared? A brief survey conducted in June and July 2011 by the author collated the details of the Barrier Examinations undertaken at each of Australia's medical schools. The results are presented in Table 1. Table 2 provides an example of the different examination formats used at Australian medical schools.

The diversity of assessment methods illustrated in Table 1 is testament to the fact that there is currently no widely-accepted benchmark for a graduating medical student, yet come January, a new brood of fresh-faced interns descend upon public hospitals around Australia to forge ahead for the next twelve months.

With new acronyms being created every year in the search for the best assessment for medical students, it begs the question – what method of assessment will best predict performance as a doctor?

This question is difficult to answer, as there is no consensus on how to measure how 'good' a doctor is. Professor Geoff McColl, of the University of Melbourne has proposed that this could be measured by intern readiness tests, performance in vocational assessments (such as college assessments), vocational and geographical destinations or even possibly Medical Board appearances. [1]

A framework known as Miller's pyramid (Figure 1) [2] goes some way towards attempting to answer this question. This 'pyramid' provides a visual explanation to the complexity of medical knowledge, and Miller advocates the evaluation of learners in the top two cells of the pyramid, in the domains of action or performance, to reflect clinical reality. [3] While MCQs can often only test the lower echelon of the pyramid, a clinical examination, such as an OSCE or Long Case, can inform on the second highest rung. A ward assessment, for example, by a supervising consultant may inform on the highest predictor of clinical competence - the implementation of medical knowledge. It is for this reason that most medical schools will have an OSCE or Long Case as part of their Barrier Examination. Table 1 shows that only one medical school (UWS) did not include a clinical examination as part of their Barrier Examinations, although this decision may be influenced by clinical examinations held in other years of their course.

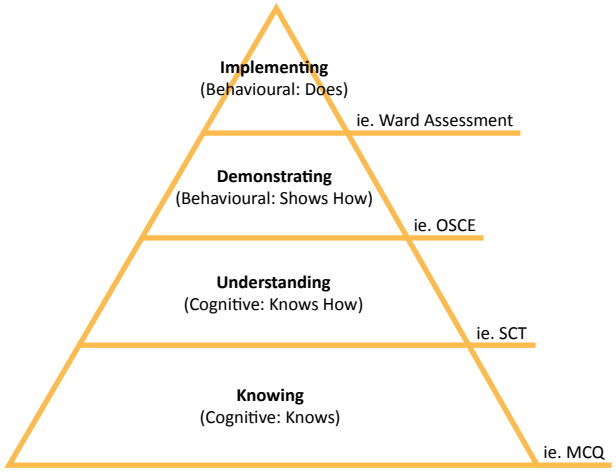

Figure 1: *Miller's Pyramid of Clinical Competence with Associated Assessment Methods. Adapted from [2], with permission.*

Research supports the notion that the OSCE is an accurate descriptor of a medical student's future performance as an intern, and does so better than other forms of assessment. [4] Yet a recent review states that between fourteen and eighteen OSCE stations are required for acceptable reliability. [5] The number of OSCE stations undertaken in the Barrier Examinations, according to Table 1, varies between six and eighteen. Some may argue that an OSCE with a lower number of stations may not be accurately assessing the aptitude of medical students.

The anxieties around the results of a Barrier Examination have been felt by any medical student applying for their first job. In France, a final year medical student's Barrier Examination results are the sole determinant of their future specialty choice – fortunately this is not the case in Australia. [6] However, many graduating medical students this year have been faced with the unprecedented effects of the 'medical student tsunami.' The Australian Government's rapid expansion of medical student numbers has led to a bottleneck at the internship level, where exponentially rising graduate doctors must battle for internship positions, which is essential to obtain registration to practice independently. Although states such as South Australia and New South Wales employ a random allocation system to assign graduating students their internship positions, if a situation is reached where some students miss out on an internship position, a merit-based allocation may become necessary. Other states, such as Victoria, already employ a merit-based allocation, and academic results form an important component of the job application process.

When a hospital selection committee reviews your Barrier Examination scores, one would hope that such results would accurately describe your clinical competence, as compared to a student from another university. The survey revealed one medical school that allowed students to resit their OSCE up to three times before failing a student, whereas other medical schools offer only one attempt at passing. With the heterogeneous mix of Barrier Examinations around Australia, many students believe there are vastly different standards for graduating medical school. Some universities grade a student with a number, while others give a letter grade or even a Non-Graded Pass. How can these parameters be used reliably to assess a student's academic

Table 1. *Results of Medical School Barrier Examination Format Survey.*

Name of Medical School	Year in which Barrier Exam is undertaken (year/length of degree)	Month of Year	Type of Examination	If OSCE (or other clinical exam if specified): Number of active stations	If OSCE (or other clinical exam if specified): Number of OSCE testing days
Australian National University	4/4	October	MCQ, Minicase, OSCE	5 (1 x Long case, 4 x Vivas)	2
Bond University	5/5	October	MCQ, SAQ, EMQ, Short OSCE, Long OSCE	15	2
Deakin University	4/4	June	MCQ, OSCE	12	1
Flinders University	3/4	November	MCQ, SAQ, OSCE	14	1
Griffith University	4/4	June	MCQ, SAQ, OSCE	10	1
James Cook University	5/6	November	MCQ, SAQ, OSCE	12	1
Monash University	4/5	November	MCQ, OSCE	16	2
University of Adelaide	5/6	November	MCQ, SCT, OSCE	12 or 18, depending on number of OSCE days	3 (Students who do not achieve a benchmark after 12 stations on Day 1 and 2, must return to complete a further 6 stations on Day 3)
University of Newcastle	Newcastle does not have any Barrier Examination testing the whole medical curriculum. Assessment is only carried out at the end of each rotation, on each specialty.				
University of New South Wales	6/6	September	MCQ, Viva, OSCE, Portfolio	9 for OSCE 8 for Viva	1 day for OSCE 1 day for Viva
University of Notre Dame, NSW	4/4	October	MCQ, SCT, SAQ, OSCE	10	1
University of Notre Dame, WA	4/4	October	MCQ, EMQ, SAQ, OSCE Portfolio	16	1
University of Queensland	4/4	November	OSCE	9	2
University of Sydney	4/4	October	MCQ, EMQ, Long Case (may be chosen from any specialty)*	No OSCE for Barrier Examinations, but for end-of-rotation assessment	
University of Tasmania	5/5	May	OSCE, Prescribing Test (+MCQ, EMQ end of 4th year)	6	1
University of Western Australia	5/6	November	SAQ, EMQ, OSCE	16	1
University of Western Sydney	5/5	June	MCQ, SAQ, SCT, MEQ	N/A – no OSCE	N/A – no OSCE
University of Wollongong	4/4	June	MCQ, SAQ, OSCE	13	1

Test Acronyms: EMQ – Extended Match Questions; MCQ – Multiple Choice Questions; Mini-CEX – Mini Clinical Evaluation Exercise; OSCE – Observed Structured Clinical Examination; SAQ – Short Answer Questions; SCT – Script Concordance Test (for more information, see Table 2).

University staff were emailed and asked to complete a brief survey on their medical school's Barrier Examination. This email was followed up by a phone call. If phone follow-up was unsuccessful, answers were sought from medical students attending the medical school.

* The University of Sydney's final year examinations focuses predominantly on topics covered over the past calendar year, rather than the whole curriculum.

worth and more importantly rank a student for job selection, in such a competitive climate?

It is not just the assessment methods, but also the timing of Barrier Examinations that differs between universities. Anecdotally, some final year medical students who undertake Barrier Examinations very close to their commencement as an intern complain that they find it difficult to cram whilst simultaneously looking for a new house, relocating to a new town and planning for graduation events. Others complain that their Barrier Examinations fall during the same period as internship applications, which may put them at a disadvantage compared to other students applying for jobs who are not facing the same stressors. Yet, having a Barrier Examination earlier in a degree may mean that the examination results may not accurately describe the student's competence when they present on their first day as an intern.

Currently, the Australian Medical Council (AMC) is the body responsible for ensuring basic standards of medical school assessment. Each medical school undergoes accreditation every ten years, or more frequently for a new school, or a school undergoing major changes to their program. The AMC also provides a pool of MCQ questions for medical schools to draw on for their assessment, which provides a double role of providing good assessment materials, as well as acting as a comparative tool between schools, and International Medical Graduates who undertake the AMC examinations. [1,7,8]

However, the calls for standardised Barrier Examinations have erupted over recent years, in Australia and around the world. [9] A

Table 2. *Examples of different types of Barrier Examinations.*

Test Name	Example of Test
EMQ	Extended Match Questions *Question: Joint Pain* *Options: A – Ankylosing Spondylitis* *B – Gout* *C – Osteoarthritis* *D – Rheumatoid Arthritis* *Instructions: For each patient described below, choose the single most likely diagnosis from the above list of options. Each option may be used once, more than once, or not at all.* *A 70-year old previously healthy farmer presents with pain on weight bearing and restricted movements of the right hip.* *A 66-year-old woman started frusemide two weeks ago and now presents with a red, hot, swollen metatarsophalangeal joint.*
MCQ	Multiple Choice Questions *What is the most common presentation of cancer of the caecum?* *A) Tiredness and fatigue* *B) Abdominal mass* *C) Small bowel obstruction* *D) Change in bowel habit* *E) Bright red PR blood*
MEQ	Modified Essay Question *You are a medical officer in paediatrics. You are asked to review a one-hour-old baby for increasing respiratory rate and subcostal recession. The baby was born at 35 weeks to a 29-year-old mother via elective LSCS. The indication for LSCS was uncontrolled BP. The mother had regular follow-up during her antenatal period. She had gestational diabetes and pre-eclampsia.* *Q1) What are the most likely diagnoses? (name two)* *Q2) What are the preliminary investigations that you would like to perform at this point? (name three)* *Q3) For each of the diagnoses list one primary pathophysiological mechanism.*
Minicase	This type of written examination question begins with a description of a patient's presentation. Students are asked questions in relation to the scenario. New information is given throughout the examination (i.e. physical examination findings, investigation results), with questions relating to the new information, however students are not allowed to go back and alter their initial answers based on new information. *Information: Brian Murphy is a 77 year-old man who presents to your surgery complaining of tiredness and dyspnoea. You note that he is pale and has signs of heart failure. His haemoglobin measures 87g/L (normal range 125-165 g/L).* *Question: Name 3 laboratory test results that would suggest the anaemia is due to haemolysis rather than reduced red cell production.* *More information: On examination you can hear crepitations at the base of each lung (indicative of fluid in the interstitial compartment of the lung).* *Question: How does fluid move into the interstitial compartment of the lung?*
Mini-CEX	Mini Clinical Examination An examiner witnesses the examinee in a clinical situation over 15-30 minutes (i.e. breaking bad news), after which feedback is given in a structured manner, using a number of marking guidelines, grading the student in different domains, such as history-taking, examination skills and communication skills. *John Brown's histology shows a melanoma with Breslow thickness of 1.4mm. Advise this patient what their histology shows and explain options for their treatment.*
OSCE	Observed Structured Clinical Examination Students rotate around a number of stations with different examiners, and standardised patients. Students are asked to demonstrate different clinical skills in each station (i.e. history-taking, physical examination, counselling). The examiner grades the student based on marking guidelines. *Sample station: John Smith is a 60 year-old man who has just returned for the results of his recent fasting lipids blood test. His total cholesterol is 6.0 mmol/L. Please counsel this patient as to the implications of this test and his suitability for statin therapy.*
Portfolio	A collection of pieces of work, including assignments, case reports and short cases.
Prescribing Test	An examination testing the ability to appropriately prescribe. *Write the prescription for a post-surgical patient's pain relief on a drug chart*
SAQ	Short Answer Questions *Outline the steps involved in the healing of a surgical incision to the skin.*
SCT	Script Concordance Testing The correct answers are determined by asking a pool of doctors to take the examination themselves. The most popular answer is awarded a '1', and any other answer is awarded a score based on how many doctors chose that answer. For example, if 20 doctors took the examination, and 15 chose '+2', and the other five chose '+1' then '+2' would received a score of '1', and '+1' would receive a score of 0.25 (= 5/20). *A 25 year-old woman presents with right-sided abdominal pain. She has vomited once today and has a low fever.* *If you were thinking* | *And you found out* | *This makes your hypothesis* *Ectopic Pregnancy* | *She has been on the oral contraceptive pill for 3 years* | *-2 -1 0 +1 +2* *Appendicitis* | *She had an appendicectomy last year* | *-2 -1 0 +1 +2* *Answer Key: -2 = much less likely; -1 = slightly less likely; 0 = neither more nor less likely; +1 = slightly more likely; +2 = much more likely.*
Viva (Voce)	A set of questions asked directly to the examinee by an examiner, over a set period of time. *An 82 year-old lady is brought to the Emergency Department by ambulance with a history of falling down in the bathroom. She is unable to stand, and is lying in bed with external rotation of the left lower limb. How would you assess and manage this patient? (5 minutes)*

strong proponent of a national Barrier Examination, the University of Queensland's David Wilkinson, believes "a national assessment (…), that all medical students could undertake, could provide some extra reassurance to the public that a certain standard has been met." [10] European medical schools have been working through the same debate since the formation of the European union which has resulted in an increasingly mobile medical workforce. [11] One author has even proposed an international licensing examination, so that doctors may truly practice anywhere they choose. [12]

This year, a new research group, the Australian Medical Assessment Collaboration, has been tasked with creating a national assessment framework over the next two years. Although this stops short of producing a national examination, it does intend to provide a guide to medical schools on what is appropriate to assess and also to share assessment resources between medical schools (something that is already being undertaken through the sharing of AMC MCQs). [1,13] In May this year, the National Assessment Forum attended by Medical Deans and representatives from the Australian Council for Educational Research (ACER) and the AMC, was held in Queensland to discuss national assessment of medical students. [10] Although a national Barrier Examination was one option discussed, other less restrictive options exist that do not stifle a medical school's opportunity for innovation, including "a scholarly collaboration between interested schools" where "results are shared, enabling generalisability." This would take the shape of a "formalised library of test items" that teachers share to "build expertise, and enable diversification." [14] Advantages would include increased ability to innovate by sharing ideas from experts in medical educators around Australia, but also economic gains, as assessors would not have to 'reinvent the wheel,' meaning that preparation for assessment could potentially become less expensive. It will be interesting to monitor the progress of this research over the next twelve months.

The Barrier Examination holds a pivotal role in medical education both as a yardstick for the public to rely on in terms of the calibre of a graduating doctor, but also as a ticket for many medical students to gain employment at their preferred hospitals. In this way, a Barrier Examination provides both a performance floor (by forcing poorly-performing medical students to repeat) and a performance ceiling (by allowing potential employers to seek out the most talented young doctors). Yet, if a national Barrier Examination is not to be implemented, further clarification is required to allow employers to adequately be able to compare results in Barrier Examinations between medical schools. Failing that, employers need to reassess the weight they place on results in Barrier Examinations for choosing their new interns.

Acknowledgements

Praveen Indraratna for his assistance in gathering the survey responses and all staff and students who responded to the survey.

Conflict of interest

None declared.

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In and out in four hours: The effects of the four-hour emergency department target on patients, hospitals and junior doctors

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Introduction

In the eyes of the general public, a hospital's Emergency Department (ED) is synonymous with overcrowding and tedious waiting. Keen to change this, last year, at the meeting of the Council of Australian Governments, the states ratified a National Partnership Agreement on health reform. One controversial outcome of this agreement was the four-hour National Access Target (NAT), which requires that all patients that present to EDs will need to be admitted, discharged or referred within four hours, if clinically appropriate. [1-3]

The new targets are currently being phased in, beginning with life-threatening triage 1 cases, but the true impact of the plan is unlikely to be felt until 2015, when non-urgent triage 5 cases will also be required to meet the target. Under the terms of the agreement, if 95% of patients within a particular Australian state are seen within the four hour target, that state will be awarded extra funding out of a national pool of $250 million over the next four years. [2]

The introduction of the NAT has been met with several questions. Does putting a time limit on patients in the ED jeopardise their safety due to rushed management decisions? Is it realistic that this target can be met when there are so many factors impeding efficient patient assessment? How will you be affected when you work against the clock in the coming years?

Problems with the NAT

Although the changes recognise the relationship between prompt treatment and better patient outcomes, the plan risks setting quantitative goals without respect to qualitative goals by forcing under-staffed emergency departments to work at an even faster pace, potentially jeopardising patient outcomes. Of concern, the four-hour plan underwent drastic modification in the United Kingdom (UK), due to concerns over patient safety. There, standards have been expanded to include eight indicators. Of the eight, only three are time-based measures, including total time in the ED. [4]

Jones & Schimansky [5] conducted a systematic review of the effects of the four-hour target in UK hospitals, and found that National Health Service spending on ED increased £820 million (1998–2007) and emergency admissions rose overall by 35% (2002–2006). Two of their most significant findings were that both time to see a treating clinician and hospital mortality remained unchanged. They also concluded that "the impact of the introduction of an ED time target and the associated massive financial investment has not resulted in a consistent improvement in care with markedly varying effects being reported between hospitals." [5]

Positives of the NAT

To the general public, the major benefit of the plan is patient satisfaction derived from shorter waiting times; however this is not as clear-cut as it seems. If a shorter waiting time is accompanied by a shorter, more abrupt consultation, will patients be more satisfied?

One major benefit of the four-hour plan is it will ultimately require

streamlining of the entire hospital system so it runs more efficiently. For example, delays in admission, imaging, pathology and consults will all need to be minimised, meaning that the NAT could be a catalyst of change for the entire hospital, not just the ED.

After conducting interviews with UK emergency physicians, Hughes [6] argued that some physicians felt that the "target gave a focus and was beneficial to EDs. It gave an incentive to improve as there was no system driver for change before its introduction." To dismiss the four-hour target entirely would be to neglect an area of medical care needing improvement - known as access block - patients who are not seen within eight hours.

The primary reason for access block is bed shortage. [7] Patients who need to be admitted often have to wait in the ED until a bed becomes available 'upstairs.' This patient occupies a bed in the ED, which thereby prevents another patient in the waiting room from being assessed. It is therefore hoped that a four-hour target will drive administrators and politicians to address the chronic bed shortage that afflicts many hospitals.

The expert panel review of emergency access targets reviewed the proposal in June 2011 and recommended that "targets must drive clinical redesign with a whole-of-hospital approach. Rather than an end in themselves, the emergency department and elective surgery targets are a tool to drive process and systemic change and a measure against which to monitor progress." [8]

Barriers to the NAT

Currently, not all patients are seen within the existing target of eight hours. For example, one major Sydney hospital, the primary teaching site for one author of this article, sees only about 70-85% of patients within the 8-hour period. If this is the case, how will it be possible to have seen and assessed 95% of patients in half that time? The rapidity of patient assessment and subsequent management is a function of the numbers of patients, staff and available beds, both in the ED and in inpatient wards. In fact, bed shortage was seen as the primary reason for failure to meet four-hour targets in the UK. [9] Unless the number of staff and beds both increase, it seems unlikely that a four-hour

target can be safely met without making sacrifices to patient care.

Furthermore, it is not just ED staff who are responsible for meeting this time limit. Inpatient teams often need to assess the patient prior to their admission, and despite being seen rapidly by ED staff, the patient may still await the services of a medical or surgical team.

Junior Doctors

The biggest concern is that linking quantitative targets to hospital funding potentially encourages staff to discharge patients inappropriately. There is a grey area between patients who require medical monitoring and those who can be followed up by their GP. Whilst it is unlikely that grossly negligent decisions to discharge will arise from the four-hour target, it is likely that the more subtle judgements will fall in favour of discharge. When the UK's National Health Service (NHS) conducted a survey of staff opinion on the four-hour target, 57% (193 out of 336 respondents) reported that patients were being discharged from ED before they had been adequately assessed to inappropriate areas or wards. [10]

The four-hour target has major ramifications on future interns and residents, who may lack the seniority to insist on the admission of a patient, and may be particularly pressured to prematurely discharge a patient. In many city hospitals, it is an expectation that junior doctors are required to see one patient per hour. This in itself is a reasonable challenge, as it includes the time taken to conduct a history and examination, as well as reading the medical records, contacting the GP for medical records and other menial but necessary tasks. Junior doctors are in the process of developing the skills of clinical judgement to organise the next step of a patient's care and navigate a complex hospital system, which is difficult enough, let alone in the face of timed targets. Time constraints will also reduce the time available for teaching from senior staff. Ideally, junior doctors should learn how to use the hospital system to meet their clinical judgement, rather than amend their clinical judgement because of a requirement of the hospital system.

Rural and Remote Australia

Rural and regional hospitals carry several additional burdens which may make it harder to reach such targets. Rural patients may have travelled several hours to reach a hospital and, when it comes time to discharge, although their clinical picture may be sound, it may not be safe for them to travel home. Hence, such patients may remain overnight in EDs out of respect to their safety, rather than the need for on-going medical care. Moreover, rural and remote patients may wait several hours for air or road transfer to a tertiary hospital, and therefore occupy an emergency room consultation room or bed. These are legitimate needs but fall outside of the four-hour target. An appropriate strategy would be to supply space and staff for patients who are in transit or who are waiting until daylight to travel home.

Data manipulation

Data manipulation of the four-hour target is also an issue. The British Medical Association survey reported that 31%, or 147 out of 471 respondents, reported that data manipulation was used as an additional measure to meet emergency access targets. [10]

When a patient presents to an ED, there are three options: discharge, admit, or refer. Referral ideally means consultation with, treatment from, and admission under a specialist medical team for definitive management. Whilst not strictly manipulating the target, referral to a surgical or medical assessment unit (MAU) will count as successfully meeting the four-hour target despite the patient not necessarily having been seen by the appropriate inpatient clinician. Furthermore, transfer of a patient to an assessment unit would actually contradict the principle of the NAT, which is to transfer patients when it is clinically appropriate to do so.

Solutions

Given the rapidly increasing number of medical graduates, some of us may miss out on prompt admission to the specialty of our choice. One possibility would be to encourage a decent portion of us to consider a path in emergency medicine. Part of this would be to create an academically and professionally supportive environment during internship and residency, and the consideration of additional financial incentives to work in this field.

EDs form one component of a plethora of acute-care services. While emergency physicians handle triage 1 scenarios such as myocardial infarcts and trauma, they also shoulder some of the burden of community medicine after hours. It is these cases which will test the four-hour limit the most. Two promising solutions are sporadically available across Australia: late night GP clinics, and "fast track" clinics within emergency departments. These clinics, often staffed by GPs, seek to divert less urgent cases away from emergency physicians proper, free up resources for more precarious cases and provide prompt service for patients that would normally wait hours to see a doctor.

However, as Richardson and Mountain point out, [11] the principle cause for overcrowding in EDs is actually access block - the delay in transferring a patient to appropriate definitive care. As such, ED waiting times reflect the interrelationship between emergency and specialist departments. Management of patient flow as a whole is what is truly likely to influence emergency waiting times.

The aim of a four-hour target is laudable and well-intentioned, but it should not be seen purely as a measure of the efficiency of the health service. It must be viewed as a driver of change, as a means rather than an end. We should not define success by the clock, rather we should be analysing patient outcomes, and the functioning of the entire hospital, not just the ground floor.

Implementation of the four-hour target carries with it a number of risks. It is of particular concern to us as future interns who may have to cope with increasing demands, leading to rushed decisions which may carry the potential of harm to the patient. Patient outcomes are the ultimate endpoint of this strategy, and of this, waiting time is only a solitary component.

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National standards in medical education: Being accountable and striking a balance

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The recent suggestions of a national curriculum and a national examination have created important discussions about Australian medical education and its future. [1-2]

The debate surrounding their merits and disadvantages is likely to remain ongoing without reaching a consensus amongst all involved stakeholders. [3]

With the significant increase in the number of medical graduates and heterogeneity of current and future medical curriculum and programmes, [4-5] there is an urgent need for regulatory authorities of medical practitioners (such as the Medical Board of Australia and the Australian Medical Council (AMC)) to ensure all Australian medical graduates have reached agreed standards of delivering adequate and safe patient care. [6]

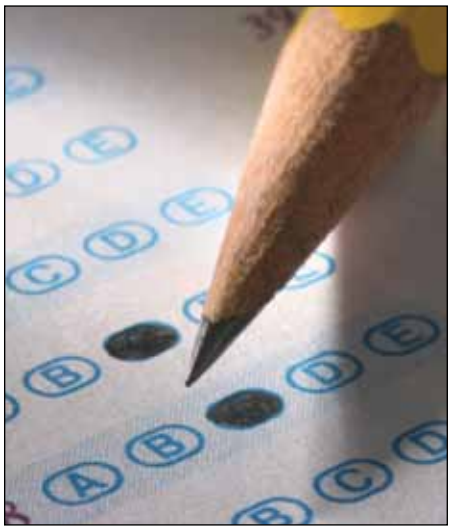
One of the most practical and effective measures that can be immediately taken by the AMC is to conduct an annual external review and audit of each medical school's final examinations. This will serve the important function of ensuring that valid and reliable assessments are being put into place. The final examinations should be properly "blueprinted" to check that the medical graduates have truly met important learning outcomes and have achieved the competencies set out in their curriculum or programmes. [7] It will also provide opportunities for the AMC to maintain the national agreed standard for Australia. [8]

The current key issues here are social accountability and patient safety, both of which are extremely important topics amongst the Australian medical education community and all state health services. [9]

The annual external review and audit of final examinations can also strike a balance, allowing medical schools to maintain autonomy over curriculum development, provided they can demonstrate that their graduates meet the national agreed standard.

Conflict of interest

None declared.



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Mental illness and medical students

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The recent article by Nguyen in AMSJ Vol 2, Issue 1 [1] raises several interesting points for discussion regarding the mental health of medical students.

In recent years, the mental well-being of medical students has received increasing publicity and coverage. This was previously a somewhat taboo topic within the medical community, but it has transitioned to become an issue that is now widely discussed and debated amongst students, faculty and the wider medical community. The outcome has been fruitful with a multitude of new initiatives highlighting the importance of mental health in health professionals. Nevertheless, there continues to be a worrying disparity in the prevalence of mental illness between medical students and the wider Australian population.

Nguyen outlined key factors that could contribute to this problem, including the fact that the medical course inflicts on students immense stressors including an overwhelming workload, rigorous examinations and lofty aspirations. [2,3] There is no doubt that this places an increasing burden on medical students. However, it must also be acknowledged that medical students generally have limited constructive coping strategies to deal with such stressors in the first place. Consequently, this may lead to a downward spiral involving concomitant behavioural problems; for example, excessive alcohol intake and the use of recreational drugs. [4]

It is a sad fact that mental illness remains widely stigmatised in the medical community. In a recent study, Hillis and colleagues [5] showed that 55% of Australasian medical students believe that there is a stigma associated with experiencing stress and distress. Nguyen and colleagues [6] conducted a multicentre survey which found that 71.6% of respondents in a survey of Australian medical students "would likely feel ashamed of depression" and that 62.1% "would not tell anyone" if suffering from depression. Not only does this indicate the medical student's reluctant attitude towards seeking help for mental illness; it also suggests that stigmatised views, along with other deterrents such as fear of confidentiality and the perceived potential impact on future career progression, can act as major barriers to medical students tackling this problem.

On a positive note, we are beginning to see an effective strategy to improve this problem that entails a coordinated, synergistic ground-up approach involving individual students, faculty, medical organisations and government bodies.

The Australian Medical Student Association (AMSA) has been playing a key role in amplifying awareness on this topic. In addition to an official policy document on well-being in medical students, an AMSA and New Zealand Medical Student Association (NZMSA) Well-being Team was formed to bring together like-minded students to brainstorm and discuss ways to make a difference in this area. Together with the assistance of faculty and students across Australia and New Zealand, this group recently launched a well-being guide entitled "Keeping Your Grass Greener," [7] to be distributed to every medical student as a first port of call for issues related to mental health and well-being. This guide aims to provide a synopsis, practical tips and anecdotes to flag the importance of well-being issues to medical students from an early stage of their career.

Students are also rising to the challenge. The Monash University Medical Undergraduates' Society (MUMUS) has adopted a well-being policy with specific goals and aims involving both staff and students. A Community and Well-being committee has also been established, which pioneers community service opportunities as well as promoting the importance of well-being in students. With this two-pronged approach, it is hoped that by serving others altruistically medical students can enhance their own well-being, as shown in recent studies. [8] Besides this, a mentorship program was piloted in 2010 involving senior medical students "buddying up" with junior colleagues. Unlike other programs, the aim was to highlight the importance of mental health and share practical experiences and tips on coping with stressors at medical school as opposed to just dealing with academic issues. An additional benefit of using a students-only approach was the openness and honesty when approaching a sensitive topic.

The old adage states that "prevention is better than cure." The focus of ongoing efforts should be to prevent mental illness in medical students rather than having to treat it a later date. An appreciation of the importance of an holistic approach to this issue will help to ensure optimal outcome for generations of medical students to come.

Conflict of interest

None declared.

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The justice of melancholia

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Although Elliot has only just started his medical journey, he has strong research interests in neurology and mental health, and is passionate about a career in neurosurgery. A concern for the health of his peers and a strong belief in the importance of good mental health for future doctors motivated him to write this article.

In a previous issue of this journal, Nguyen [1] succinctly identified a high incidence of mental health conditions in Australian medical students.

The increased rates of depression and suicidal ideations experienced by this population depict a bleak future for the medical profession in this country. Of great concern is the fact that the barriers preventing medical students from accessing support are not only unique, but despairingly fraught with immeasurable difficulty and stigmatisation; stigma that is entrenched and perpetuated through the core of the medical culture. [2] Despite our existence in an apparently enlightened and diverse cultural framework, the disconcerting stigma branded upon mental health exists and it is truly deplorable.

Pupils of the medical profession recognise that discrimination against mental health issues dwells not only in the general medical community, but also within their school. [2,3] Students believe that notifying the medical school of a depressive episode could result in the loss of the faculty's respect [4] and the affected being labelled as 'weak.' [5] These perceptions result in a general hesitancy and fear for medical students of disclosing any symptoms that may reflect an issue of mental health to their school or hospital. Indeed, the moniker of 'weakness' discourages students from reporting mental health issues so as to not affect their chances of future employment in a climate where post-graduate intern positions are at an all-time low. [6] Though such a fastidious designation of discriminatory labels and 'black marks' may not be performed by the medical community, the important issue here is that this belief exists within the student body, thus presenting a significant barrier to support for those who struggle with depression.

The aversions and insecurities medical students hold towards approaching support services can be surmised by concerns of discrimination, professional consequences and above all, confidentiality. Sections of the literature have reported that students do not trust that they will receive confidential care when accessing services for depression. [7,8] Indeed, medical students have been found to display staunch apprehension and reluctance in approaching clinical tutors with mental health issues, [9] fearing that these individuals could breach confidential care and notify the medical school. As clinical tutors are frequently delineated as ubiquitous pillars of support by universities, these attitudes and beliefs demonstrate a severely declining trust in inherent supportive frameworks offered by the medical academia.

Though these convictions of mistrust held by medical students may seem nothing more than a bout of widespread paranoia, substance has recently been injected into the heart of these fears. The new Health Practitioner Regulation National Law Act (the National Law) [10] stipulates that all health professionals and education providers (i.e. medical schools) must report students who are 'impaired,' by mental health conditions or otherwise, to the National Agency. This legislation has made it a legal requirement to violate the trust of medical students who seek support for depression, thereby encouraging breaches of confidentiality against a demographic at a greatly increased risk of not only depression, but also of suicide. [4] Such a disposition lends credence to the fears that medical students have in accessing mental health support services as previously described.

Mandatory reporting presents a very tangible likelihood for allocations of the dreaded 'black mark.' The identification of affected students, coupled with the stigma it entails, potentially tarnishes academic records, desecrates hopes for future employment and turns

suicidal ideations into reality. The shameless National Law produces the most shocking barrier to support, punishing students who seek a professional confidant in light of debilitating psychological sequelae. This law represents an unmerciful dereliction of duty that governmental agencies should have for student welfare.

Though mental health has ascended into the list of National Health Priorities, [12] the implementation of the National Law demonstrates a complete disregard for those individuals who are at great risk of serious psychological effect. This obtuse legislation represents the ultimate hindrance and opposition for students to assume the most basic of human rights: trust, comfort and confidence in their ability to seek health advice.

Thus, the widespread belief amongst medical students that a disclosure of depression will result in a permanent blemish on their future career prospects has been confirmed by the National Law. Pathways for the identification, reporting and subsequent exclusion of depressed medical students has been entrenched in the legal dogma of this country. The stigma that surrounds mental health has been expressed, personified and consolidated in this damning legislation and has eloped with the law.

Conflict of interest

None declared.

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Onsite and offsite use of computer aided learning in undergraduate radiology education

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Winnie completed her research year in July 2010 at the National University of Singapore. She is currently completing her clinical studies in Ballarat and Western clinical school. She is interested in rural health, and hopes to be involved with medical education and medical writing in the future.

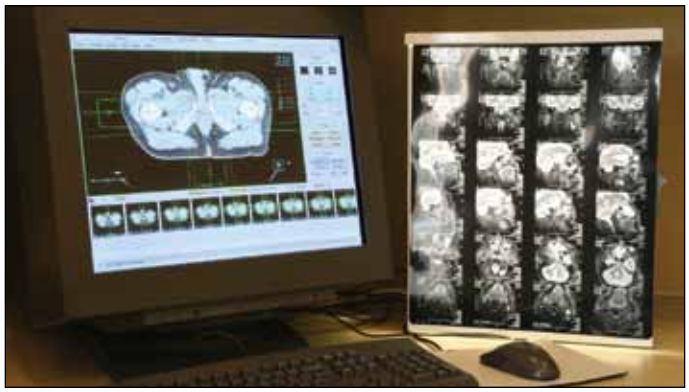
Aim: Computer-aided learning (CAL) is considered comparable to traditional media for undergraduate radiology teaching. Previous studies have often compared the efficacy of traditional media to onsite CAL use, yet real world usage of CAL is likely to occur in offsite settings. This study aims to compare usage and learning outcomes of a chest radiology CAL in onsite and offsite settings. **Methods:** Participants were fourth year medical students (n=52) at the National University of Singapore (NUS) undertaking one week radiology rotations. Students were randomly allocated to complete a web-based chest radiology CAL onsite, or offsite at a time and place of choice. Pre- and post-tests were taken to measure knowledge gain, and a questionnaire was used to explore student usage and preferences. **Results:** The onsite CAL group demonstrated significant knowledge gain (+15.8%, $p<0.05$) whilst the offsite group did not (+5.8%, $p>0.05$). However, the difference between the groups was not statistically significant ($p=0.069$). Total time spent and completion of the program was similar between the two groups. Yet, questionnaire results showed that the offsite group multitasked more and appeared to have poorer concentration. A majority of students from both groups preferred the convenience of offsite CAL use over onsite CAL use. **Conclusion:** A significant difference between the test groups was not observed, although there was a trend toward onsite CAL use being more effective. In planning CAL teaching, particularly for offsite use, educators need to provide sufficient support and integration for an optimal outcome.

Introduction

Chest radiology is important for acute and emergency management, and is therefore an essential learning component of undergraduate radiology teaching. [1] However, studies show that chest radiology competency amongst graduating medical students is poor. [2,3] Poor competency is attributed to lack of formal teaching of radiology in the curriculum. [2,3] Worldwide, radiology teaching is compromised by limited formal teaching in a hectic curriculum, and competing demands on radiologists. [4,5]

Computer aided learning (CAL) has been advocated as a potential tool to alleviate some of the limitations in radiology teaching. [6] CAL is time and cost effective for educators, [7] and especially useful in an image rich specialty such as radiology. To evaluate the effectiveness of CAL for transferring knowledge gain, previous studies have undertaken media comparisons between CAL and traditional learning, such as lectures or tutorials. Individual studies in radiology and non-radiology medical education [8,9] demonstrate that overall, knowledge gain with CAL is comparable to traditional media. [6,7,10] However, critics have repeatedly advocated for a shift of focus – away from the debate of whether CAL is superior, to research using CAL to CAL comparisons, and on how CAL can be used effectively in the curriculum. [11,12]

The majority of media comparison studies in undergraduate medicine have limited CAL usage to a controlled onsite session. In these studies, the study design consisted of a pre-test, CAL or traditional learning, followed immediately by the post-test – therefore, usage of CAL outside a single session was not possible. [6,8-10] This is paradoxical, as CAL is valued by students and educators alike for its flexibility and convenience of access offsite. [7]



Education literature have promoted student-centered learning to be useful for deep understanding, and flexibility to be useful for developing self learning skills in an era where information is rapidly updating. Further, due to the web-based nature of recent CAL programs, access is unlikely to be restricted to a single session. In an attempt to emulate "real world" use of CAL, Devitt, Palmer and Hudson used a different study design whereby students were given free access to a CAL program for a period of two weeks. [13,14] Third year students were permitted to use the CAL program at a time and place of choice. The experience with offsite learning showed access logs of some students failing to access the program at all; yet some of the same students were willing to attend scheduled pre- and post-tests. [14]

Aims of the Study

In light of prior experiences with offsite CAL use, whether knowledge gain between traditional media and CAL is still comparable when CAL is used offsite becomes a relevant question to explore. Using a CAL radiology courseware, our study aims to compare usage and knowledge gain in onsite and offsite settings for undergraduate students.

Methods

The program

The "Radiology Courseware" created by the radiology department at the National University of Singapore (NUS) is a CAL program with 102 electronic pages, and covers principals of chest radiology interpretation and common pathology. It was created to supplement undergraduate teaching.

Subjects

All fourth year clinical students undergoing their one week radiology rotation in October 2009 (n=52) were invited to participate in the study (Figure 1). Traditionally, fourth years received a didactic lecture on chest radiology. Students in this study were given a web-based chest radiology (chest x-ray; CXR) CAL program to complete and a supplementary chest radiology lecture after completing pre- and post-tests.

Prior to the rotation, the radiology department allocated ten clinical groups (n=5 or n=6 per group). For the purposes of this study, each clinical group was evenly allocated into either group A or group B by alternation. Group A completed the chest radiology CAL program onsite in the department library during an allocated two hour session. Group B were given one week to complete the same CAL program offsite, at a time and place of choice. Participating students provided informed consent.

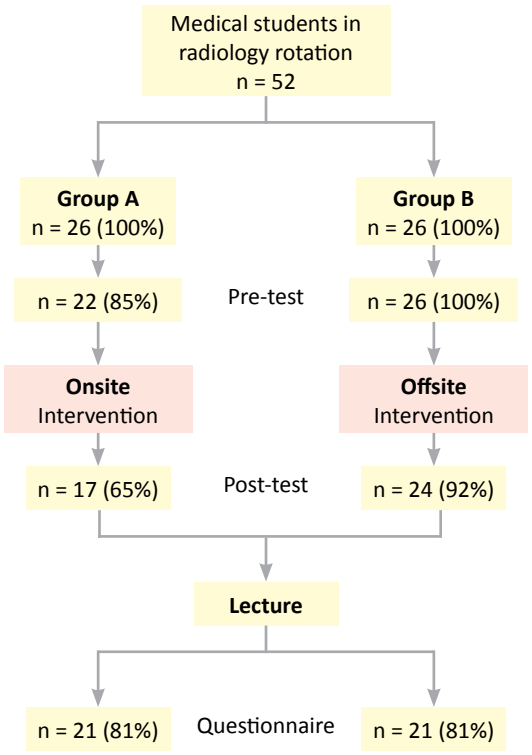


Figure 1. *Study design and participants.*

Pre- and post-tests

Pre- and post-tests were completed at the start and end of the rotation week, respectively. The pre- and post-test were derived from the chest radiology CAL program content and consisted of thirteen multiple choice questions. Blueprinting ensured that areas of knowledge tested were proportional to the CAL content and concordant with intended chest radiology learning outcomes for clinical students. For radiograph interpretation questions, only standard teaching images from the program itself were used. The test was reviewed and approved by a senior radiologist.

The pre- and post-tests covered similar topics, but differed in content. Although identical tests would ensure equal difficulty for pre- and post-tests, it may also increase the likelihood of students performing better in the post-test, simply as a result of participating in the pre-test. The pre- and post-tests were piloted on elective medical students and were rated to be of comparable difficulty. The tests were collectively administered on PowerPoint projections to provide good image visibility, and a standardised test setting for the students. Students were required to work individually. Pre- and post-tests were matched by de-identified codes.

Questionnaire

At the end of the study a questionnaire was given to each participating student. The questionnaire included questions on demographics, onsite and offsite usage patterns, and student preferences for setting. The questionnaire was modelled after similar qualitative evaluations of CAL from previous studies. [6,8] Questions regarding impact of setting on learning and motivation were based upon psychology and education learning theories. [15,16] Computer usage and CAL attitude questions were based on previous computer attitude surveys. [17-19] A combination of open and closed question techniques were used. Most closed questions were in a 5-point Likert scale form with responses from “strongly agree” to “strongly disagree.” Open questions were used for greater exploration of student attitudes and preferences, and the reasoning behind their opinions. The instrument was piloted together with the pre- and post-tests. Poorly phrased questions eliciting ambiguous answers were excluded or revised.

Statistical analysis

Data was entered into Microsoft Excel and analyses were performed using SPSS 17.0 created by IBM (New York, USA). Descriptive results were presented for the questionnaire, and pre- and post-test results were analysed by within group (Wilcoxon signed rank test) and between group (Mann Whitney U test) comparisons. Raw scores were converted to percentages for easy interpretation. A p-value of 0.05 or less was considered to be statistically significant.

Ethical approval

This study was exempt from NUS Institutional Review Board as it was an educational settings research without identifiers. The project was approved by the Head of Department at NUS, Department of Diagnostic Radiology, and the Dean for Yong Loo Lin School of Medicine.

Results

Demographics

Overall participation was high for the pre-test, post-test and questionnaire. For the questionnaire, group A and group B both had a response rate of 81%. For pre- and post-tests, participation was higher amongst group B students (Figure 1). Student demographics for age and gender were similar between the two groups (Table 1).

Table 1. *Summary of student demographics.*

	Gender		
	Male	**Female**	**Average age (years)**
Group A (onsite)	57.1%	42.9%	22.19
Group B (offsite)	61.9%	38.1%	22.10
Total	59.5%	40.5%	22.14

Pre- and post-test results

The scores obtained by students ranged from 38.5 to 100% for both pre-test and post-test scores. Pre-test scores were significantly lower in group A compared to group B ($p<0.05$). Pre- and post-test differences showed that the knowledge gain in group A was statistically significant, but the knowledge gain in group B was not statistically significant (Table 2). Between-group comparisons show that group A had a 10.0% larger mean improvement than group B, but this was not statistically significant ($p>0.05$).

Table 2. *Summary of pre- and post-test results.*

	Pre-test	**Post-test**	**Improvement**
Group A (onsite)	69.7±6.1	85.5±8.0	15.8±9.3*
Group B (offsite)	78.5±3.8	84.3±4.2	5.8±6.8**
Difference	-	-	10.0±10.9***

**p=0.005, **p= 0.109, ***p=0.052*

Usage and completion

Total time spent on the chest radiology CAL was measured via student self reporting on the questionnaire, and observation of the onsite group. The two groups reported similar duration of use, with 46 minutes average for Group A, and 47 minutes average for Group B. Self reported completion of the chest radiology CAL was also similar across both groups (Table 3). The entire CAL program was completed by 71.4% of students in group A and 66.7% of students in group B and a proportion of students in both groups A (23.8%) and B (19.0%) completed half, less than half or none of the chest radiology CAL.

Table 3. *Total amount of CAL completed.*

	None	**< Half**	**Half**	**> Half**	**All**
Group A	0.0%	4.8%	23.8%	0.0%	71.4%
Group B	4.8%	9.5%	9.5%	9.5%	66.7%
Total	2.4%	7.2%	16.7%	4.8%	69.1%

Motivation, distraction and multitasking

Self reported motivation levels were moderately high and similar between group A and B (Figure 2). Most students selected "agree" (52.4% in group A, 61.9% in group B) or "strongly agree" (19.0% in group A, 14.3% in group B) to the statement that "I was motivated during the CAL session." Overall distribution of responses to the statement "I was distracted during the CAL session" was similar across all options (Figure 3). Notably, a higher proportion of group A respondents (33.3%) strongly disagreed that they were distracted during the chest radiology CAL compared to in group B (4.8%). Conversely, more respondents in group B (23.8%) than group A (4.8%) strongly agreed that they were distracted during the session.

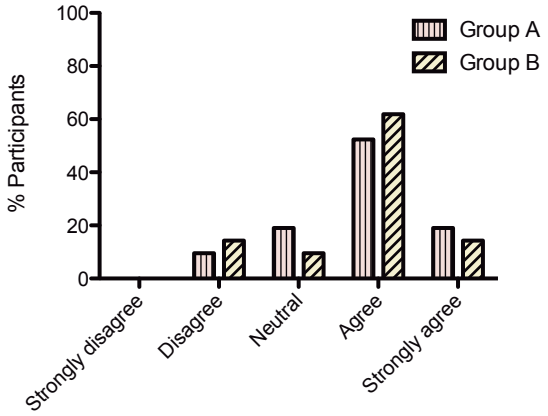


Figure 2. *Motivation during the CAL session ("I was motivated during the CAL session").*

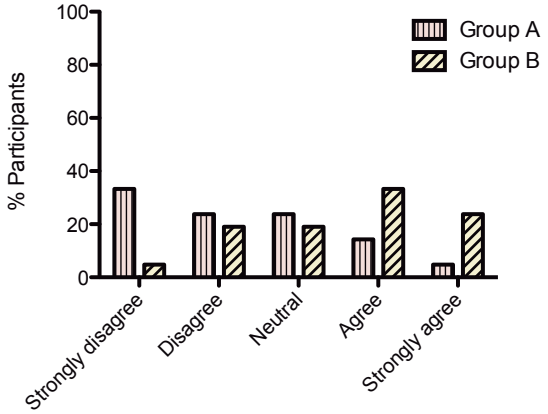


Figure 3. *Distraction during the CAL session ("I was distracted during the CAL session").*

Finally, multitasking, such as use of instant messengers, and social network websites during CAL, was used as an additional criterion for assessing motivation and distraction. As with the previous question on distractions during CAL, responses to the statement "I was multitasking during the CAL session" also ranged from highly agree to highly disagree (Figure 4). However, a distinct pattern to the question was seen with the majority of group A students strongly disagreeing (52.4%) or disagreeing (33.3%), and the majority of group B students strongly agreeing (38.1%) or agreeing (38.1%) to the statement.

Preference for setting

The most popular chest radiology learning method in both onsite group A (90%) and offsite group B (61.9%) was the "both CAL and lecture" teaching, compared to "CAL only" or "lecture only" teaching (Figure 5). Explanation given for wanting to complete CAL offsite included freedom, flexibility and convenience to complete the task at one's "own time, own target." Reasons given for preferring to access CAL during scheduled sessions included being "forced" to complete the task, having a tutor present and the ability to discuss learning with peers.

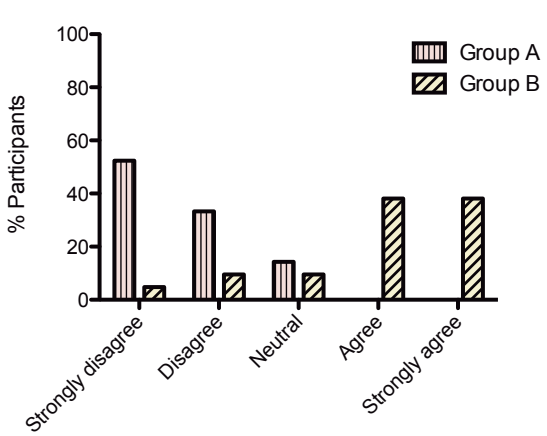


Figure 4. *Multitasking during the CAL session ("I was multitasking during the CAL session").*

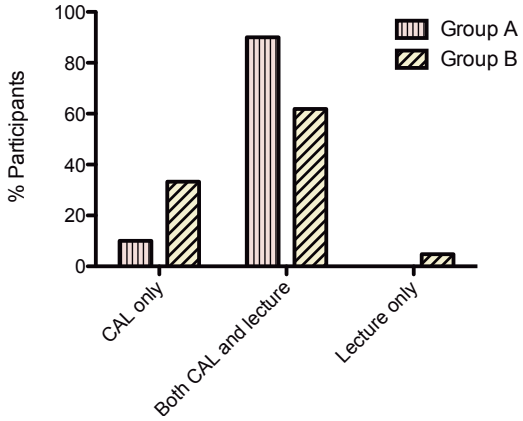


Figure 5. *Preferred method for CXR learning.*

Discussion

Previously, CAL studies have predominantly occurred in an onsite setting, where access was controlled to a single, scheduled session. This prospective, randomised study aimed to test the hypothesis that onsite and offsite access of CAL differed in usage and learning outcomes.

Pre- and post-test results

Pre- and post-test differences demonstrated a statistically significant ($p<0.05$) improvement in chest radiology knowledge for students in the onsite CAL group. Offsite CAL students also gained knowledge, but this was not statistically significant. Between-group comparison showed that knowledge gain was greater onsite than offsite, but this was also not statistically significant.

Searches of Pubmed and ERIC databases of articles up to December 2009 did not reveal any previous studies investigating learning outcomes in onsite and offsite CAL settings. Nevertheless we can understand the results of this study better in light of previous studies comparing CAL to CAL learning outcomes. Maleck *et al.* studied third year medical students (n=225) in a comparable pre- and post-test design. Their results showed post-test improvements of 11.2% and 15.1% ($p<0.05$ for both), after non-interactive and interactive CAL, respectively. [6] A separate study of similar design in third year medical students (n=100) showed neuroradiology knowledge improvements of 16%, 17% and 21% ($p<0.05$ for all) for didactic, problem solving and free text CAL, respectively. [14] Considering these results, the onsite improvement of 15.8% ($p<0.05$) in this study is equal, whereas the offsite improvement of 5.8% ($p>0.05$) is smaller in magnitude compared to previous studies.

Usage of chest radiology CAL

Usage results contradicted the hypothesis that there is a difference between onsite and offsite groups in duration of use, and amount

of CAL completed. Average time spent in the two groups was almost identical. In contrast, Devitt and Palmer's interactive to non-interactive CAL study showed a difference of up to 50 minutes in average duration of use between different CAL groups. [13] Hudson's study also showed up to twenty minutes difference in average time spent on CAL between different CAL groups. [14] Previous studies did not directly investigate the amount of CAL completed, but based estimations on login data. Based on login data, Hudson concluded that there were students who failed to use the CAL program at all. [14] Using student reported data, this study also identified individuals from both groups who completed little or none of the chest radiology CAL. Overall, 69% of all students completed the entire CAL, and this was similar between the onsite and offsite groups.

Though time spent on CAL was similar between onsite and offsite groups, the quality of time spent may have contributed to differences in knowledge gain. Student in onsite and offsite settings self reported similar levels of interest and motivation for CAL. However, more students in the offsite group agreed to the statement that "I was distracted during the session." Moreover, multitasking, such as checking emails and news online, was distinctly more prevalent in the offsite group. Onsite students may be motivated to use CAL through influence of tutors, peers undertaking similar tasks, and by being physically present in a learning environment. [20] On the other hand, offsite CAL is akin to distance learning, which is more difficult to motivate and monitor. [20] Despite apparent difficulties in concentration offsite, the majority of students preferred to complete CAL offsite rather than onsite. Students found the flexibility and "own time, own target" capacities of CAL particularly attractive in a busy medical curriculum.

Limitations

The initial pre-test results in the offsite group were higher than that of the onsite group, and may have contributed to the smaller post-test improvement in the offsite group. However, the offsite group appears to have had room for measurable improvement in this study, as students achieved up to full marks in both pre- and post-tests.

Sample size was limited by the use of radiology rotation students at a single site, and this limited the possibility of a control group, and the ability of the study to demonstrate statistical significance. Volunteer recruitment from the entire cohort may have provided a larger sample size, but is also likely to introduce selection bias. Recruiting students from other teaching hospitals may confound results as radiology teaching content differs between each hospital. Another limitation in the sample was that pre- and post-test participation was higher in group B than group A, and it is difficult to determine whether selection bias occurred.

Our study only tested for short term chest radiology knowledge gain. Some researchers have used a delay test method to test knowledge retention, and long term effects of CAL interventions. [21] In this study, a post-test was performed in the same week as the CAL intervention because differences in clinical exposure and teaching subsequent to the radiology rotation may confound knowledge gain.

Usage data was mainly drawn from the questionnaire. Consequently, honesty of student feedback is a potential limitation. To encourage honest answers, the questionnaire was anonymous and non-judgmental wording was used. Another limitation of the questionnaire was that no statistical demonstrations of reliability were available.

As with previous studies, this study faced challenges in balancing internal and external validity. [14] Some researchers limited student interaction, requiring students to use CAL individually. [9,13] In many onsite studies, usage outside of allocated sessions was also impossible, as the posttest was scheduled immediately after CAL intervention. In contrast, this study did not control peer interaction, and free access of CAL was permitted outside of scheduled sessions for the onsite group. Although internal validity is reduced, we used this methodology to allow investigation of student usage and learning outcomes of CAL in "real life" onsite and offsite settings.

CAL setting was categorised into two broad settings for the purposes of the study. We recognise that categories of settings need not be limited to onsite and offsite settings. Learning style and needs also varies between students, between institutions and even within a single cohort. Within the students in this study, a range of preferences and attitudes towards CAL was seen. Clearly, recommendations from this study may not benefit all students; for example, highly self motivated students are less influenced by external motivational factors, [16] and for these students, setting would be unlikely to result in differences in CAL usage and learning.

Conclusion

This study addresses an unanswered question in CAL literature regarding the differences in usage and learning between different CAL settings. According to use of setting in studies to date, CAL use was categorised into onsite and offsite settings. The results showed that the onsite setting discouraged multitasking and may have produced greater knowledge gain. Yet there is great potential for CAL use in medical teaching due to its flexibility and accessibility outside a physical classroom.

Together with previous researchers, [8,14] we recommend that implementation of offsite CAL use needs to be carefully supported and planned into the curriculum. Improvements to integration may include setting deadlines, use of electronic or face to face reminders to complete CAL, and implementation of assessments for evaluation and feedback. In particular, experience with medical students shows that formal assessment is important in motivating effective CAL use. CAL can be used together with traditional learning; as students suggested, basic information can be provided by CAL, followed by a subsequent summary lecture where questions can be addressed. Alternatively, tutors can answer questions by invitation of email questions, and incorporate frequently asked questions for future reference. [8]

Further investigation is needed to understand and optimise CAL use in medical teaching. For example, CAL use and outcomes with and without tutor feedback can be compared. Furthermore, ongoing monitoring of usage and learning outcomes is required as new CAL curriculums and technologies are developed and implemented.

Acknowledgements

The chest radiology courseware used in this study was developed by staff of the National University Singapore (NUS) Department of Diagnostic Radiology. I thank my supervisor, Dr. Goh Poh Sun for his guidance, and Dr. Chan Yiong Huak for his statistical advice.

Conflict of interest

None declared.

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Maternal attitudes towards breast and bottle feeding in a regional community

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Jacqueline completed her undergraduate degree at Sydney University in B.Applied Science (Leisure and Health). She has a particular interest in women's health and health education.

Background: Based on research demonstrating the many benefits of breastfeeding, it is recommended babies be exclusively breastfed from birth to at least six months of age. However, despite these known benefits, many women choose to bottle feed or cease breastfeeding before six months. **Aim:** To survey women in order to determine factors associated with their attitudes and choice to bottle feed or breastfeed their children, with the aim of identifying areas to target education to improve breastfeeding rates or duration. **Methods:** Anonymous surveys were distributed to a convenience sample of 106 adult female patients selected from a suburban general practice. MS-Excel and Epi Info 3.5.3 software package were used for data management. Chi square was used for analysis. **Results:** The response rate was 94.3% (n=100). There were trends suggesting an association between income and the respondents' choices (p=0.26); and income and the respondents' mothers' choices (p=0.51). Respondents were significantly more likely to choose the feeding method their own mother used (p=0.01). **Discussion:** Income and respondents' mothers' choice regarding breastfeeding were identified as factors possibly associated with respondents' attitudes and choice. Hence awareness of individual family dynamics may assist in targeting prenatal education to help increase rates of breastfeeding. A large proportion of respondents chose to bottle feed and also believed that the bottle was as good as breastfeeding. The needs of this group also need to be met. **Conclusion:** To increase breastfeeding rates, individualised prenatal education as well as supporting women through their breastfeeding problems is a likely requirement.

Introduction

In Australia, the National Health and Medical Research Council (NHMRC), in agreement with the World Health Organisation (WHO) guidelines, recommend exclusive breastfeeding from birth up to six months of age. [1,2] Exclusive breastfeeding means breastfeeding only, with no complementary bottle feeds. Breastfeeding is recommended to be continued for up to two years and beyond. [3]

There are many benefits of breast feeding for mother, child and society. For the baby, breast milk assists with immune system development, thus reducing the risk of morbidity and mortality. [1] Breast milk also reduces the risk of obesity in childhood, [4,5] chronic diseases, [6] Sudden Infant Death Syndrome (SIDS), [7] childhood cancers [1] and psychiatric disorders. [8] Additionally, there is some evidence that being breastfed may reduce the incidence of high cholesterol and hypertension. [9] Breastfeeding can improve eyesight [10] and cognitive development with an increase in IQ of 2-5 points on standard IQ tests. [11-14]

For the mother, breastfeeding promotes infant bonding and attachment. [1,15] It also leads to quicker recovery after childbirth, reduces risk of ovarian cancer and possibly reduces the risk of breast cancer, post-menopausal hip fractures, osteoporosis and maternal depression, although further research is required. [16,17] Breastfeeding also reduces the risk of having another baby within a short period of time. Short intervals between pregnancies may lead to adverse outcomes as the mother's nutritional reserves need at least eighteen months to be restored. [18,19]

In terms of society and the economy, studies have shown that if an infant is not breastfed or is weaned prematurely, there are increased healthcare costs for associated illnesses. [1,20] Breast milk is free whereas formula is not. [21] Environmental benefits to society result from reduced waste associated with the production, transport and packaging of artificial baby milk, bottles and teats. [22]

However, despite these benefits there are concerns that breastfeeding rates are far from optimal. Studies have shown that in Queensland, only 10% of children were exclusively breastfed at five months of age. [1,23] In Western Australia and New South Wales (NSW) children aged zero to four years were exclusively breastfed for six months or more at a rate of 12% and 18% respectively. [1,20,24] There is evidence that the rates of breastfeeding are not uniform across socioeconomic areas. In the 2005-06 NSW population health survey, exclusive breastfeeding of children at six months of age was statistically lower for infants with mothers without tertiary qualifications, from lower socioeconomic areas and in those aged younger than 25 years. [1,24] Women from higher socioeconomic groups were more likely to breastfeed and continue breastfeeding for longer than women from lower socioeconomic groups. [25-29]

In 2005, a project was approved to develop a set of national priority Headline Indicators to monitor the health, development and wellbeing of Australian children and to explore processes to facilitate ongoing data collation, analysis and reporting. One of these priority areas is the proportion of infants exclusively breast fed at four months of age. The Australian Institute of Health and Welfare (AIHW) has identified a lack of current national data providing information on the proportion or duration of infants exclusively breastfed. [1] The Australian Bureau of Statistics (ABS) has also identified the need for further research regarding the prevalence and duration of breastfeeding. [1,30]

Therefore, whilst the importance of breastfeeding is well recognised, data on breastfeeding rates and research on factors and attitudes associated with choice of feed are limited. This project is warranted to quantify and explore these under-researched issues.

Methods

This project received approval from the Human Research Ethics Committee at The University of Wollongong.

Materials

Development of the survey tool was informed by identifying independent variables of likely influences for feeding choice selected from a review of the literature. [19,22,25,31-34] The survey was formed through the use of multiple choice check boxes to allow ease of question answering; however there was an opportunity for free writing comments. The survey was then piloted for acceptable readability by a research supervisor, a practice doctor and a few patients.

Data collection

Surveys were collected over a two week period during normal business hours for the medical centre. Inclusion criteria to the study were: females between the ages of 18 and 50, who lived in postcode 2530 and had children for whom they had to make a choice of feeding type. Participants were identified through opportunistic questioning at an Illawarra Medical Centre. One hundred-and-six surveys were distributed. The aim of the research was explained to the participants and if they were interested in participating, a participant information sheet was given. If they agreed to proceed, an anonymous survey was given for them to fill out. Women had the choice to not complete the survey after they had seen it. These surveys were shredded appropriately. Completed surveys were collected by the researcher, who returned to collect the survey after five minutes, ensuring a high proportion of returned surveys.

Table 1. *Sample attributes.*

Characteristics	n (%)
Age	
18-25	7 (7)
26-30	20 (20)
31-35	20 (20)
36-40	19 (19)
41-45	15 (15)
46-50	19 (19)
Marital status	
Single	13 (13)
Separated	6 (6)
Defacto	21 (21)
Married	60 (60)
Education	
< Year 10	10 (10)
Year 10	32 (32)
Year 12	13 (13)
TAFE	34 (34)
Undergraduate	6 (6)
Postgraduate	4 (4)
Blank	1 (1)
Income	
<$25k	19 (19%)
$25k - $50k	24 (24%)
$50k -$75k	25 (25%)
$75k +	30 (30%)
Blank	2 (2%)

Table 2. *Infant feeding choices.*

Respondents'	n (%)
Choice of feeding	
Bottle	32 (32)
Breast	43 (43)
Mixed/swapped	25 (25)
Believe to be better	
Bottle	4 (4)
Breast	72 (72)
Same	22 (22)
Blank	2 (2)
Time	
<1 month	23 (23)
<3 months	18 (18)
<6 months	15 (15)
<1 year	15 (15)
<2 years	6 (6)
≥2 years	1 (1)
Blank	22 (22)
Mother's choice	
Bottle	37 (37)
Breast	39 (39)
Mixed	10 (10)
Unsure	14 (14)

Analysis

Quantitative data from the survey were entered into MS-Excel (Microsoft Corporation., Washington, US) and then imported into Epi Info 3.5.3 (Centers for Disease Control and Prevention, Atlanta, US) for analysis. The Chi square test was performed to determine the statistical significance in differences in proportions.

Results

Of the 106 surveys distributed, four were not returned and two were excluded due to conflicting responses, resulting in 100 surveys being included in the data analysis with an effective response rate of 94.3%. Conflicting responses were due to selection of bottle feeding as their choice of feeding method; however respondents had also checked boxes for time breastfeeding.

There was a generally even distribution of respondents across six age groups, other than the 18-25 years age group which was relatively under-represented with 7% (n=7) of respondents. Over three-quarters of the sample (81%) were in a defacto or married relationship. Over half (61%) had a year 12, TAFE or University education (Table 1).

Forty-three percent (n=43) of the respondents chose to breastfeed, yet 72% (n=72) of the sample believed breastfeeding was best. The proportion of respondents breastfeeding declined with increasing time from delivery with 23% (n=23) breastfeeding for less than one month, 15% (n=15) less than one year and only 1% (n=1) breastfeeding for more than two years. The choices of the respondents' mothers regarding breastfeeding were nearly evenly divided with 37% (n=37) choosing to bottle feed and 39% (n=39) choosing to breastfeed (Table 2).

Respondents could choose multiple options for four questions in the survey: reasons for bottle feeding, reasons for breastfeeding, reasons for stopping breastfeeding and sources of information. Most reported reasons for bottle feeding were that the baby was still hungry (n=26), that milk did not come through (n=16) and that breastfeeding hurt (n=15) (Figure 1). Reasons for breastfeeding most commonly reported

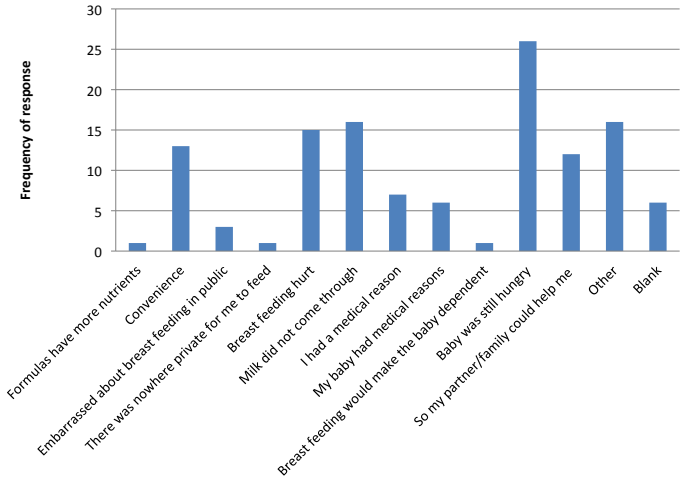

Figure 1. *A graph indicating reasons for bottle feeding.*

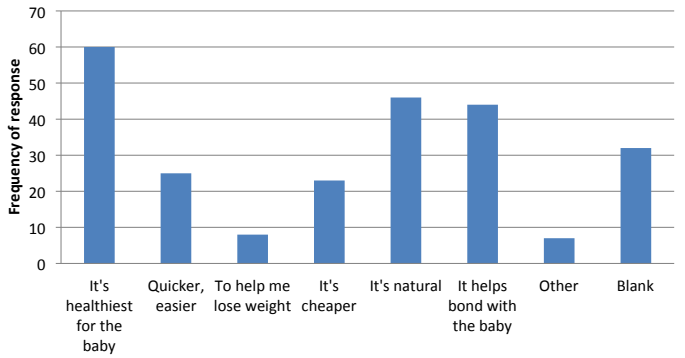

Figure 2. *A graph indicating reasons for breastfeeding.*

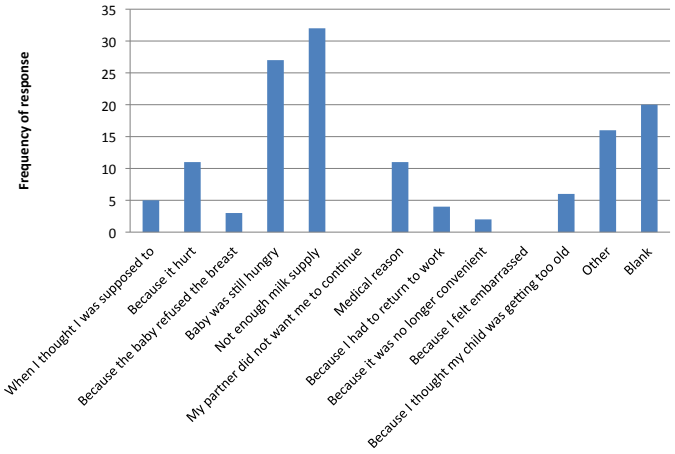

Figure 3. *A graph indicating reasons for stopping breastfeeding.*

were that it was perceived to be healthiest for the baby (n=60), natural (n=46) and that it helped bonding with the baby (n=44) (Figure 2). The most common reasons for stopping breastfeeding were due to low milk supply (n=32), because the baby was still hungry (n=27), because breastfeeding hurt (n=11) and for medical reasons (n=11) (Figure 3).

Regarding breastfeeding information, 74% (n=74) believed they had enough information; 21% (n=21) felt they did not get enough information and would have liked more, and 2% (n=2) stated that they did not get enough information but did not want to know any more. The most reported source of information was from a midwife or lactation consultant or early childhood nurse. This was followed by the antenatal clinic and a doctor (Figure 4).

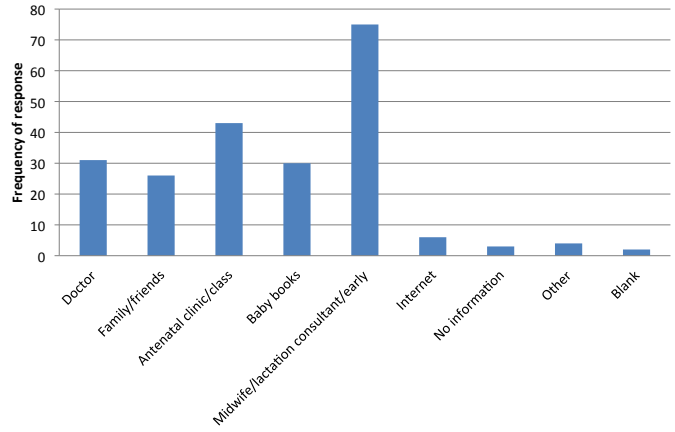

Figure 4. *A graph indicating information sources.*

All but one of the 18-25 year old women bottle fed or mixed/swapped. Of those whom tried to breastfeed in this age group, the maximum duration was less than three months. No respondents under 35 years of age breastfed beyond one year. Breastfeeding rates were highest in 26-30 year olds and in those with higher incomes (Figure 5).

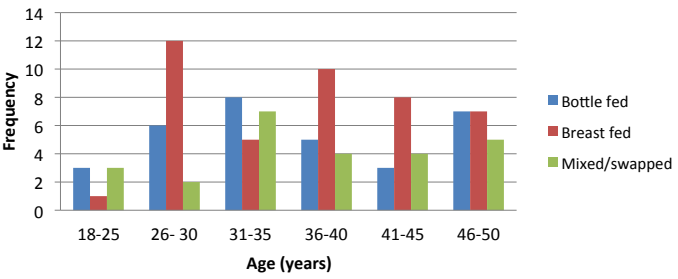

Figure 5. *A graph indicating the choice of feed in age distribution.*

The <$25,000 income group produced the lowest number of respondents who breastfed, although the difference between this group and the others was not statistically significant (chi square 4.179, df 3, p= 0.24). Of those with an income of less than $25,000, seven chose to breastfeed and eight chose to bottle feed, compared with those with an income of $75,000+ where fifteen chose to breastfeed and eight chose to bottle feed. However, this difference failed to reach statistical significance (chi square 1.282, df 1, p=0.26) (Figure 6).

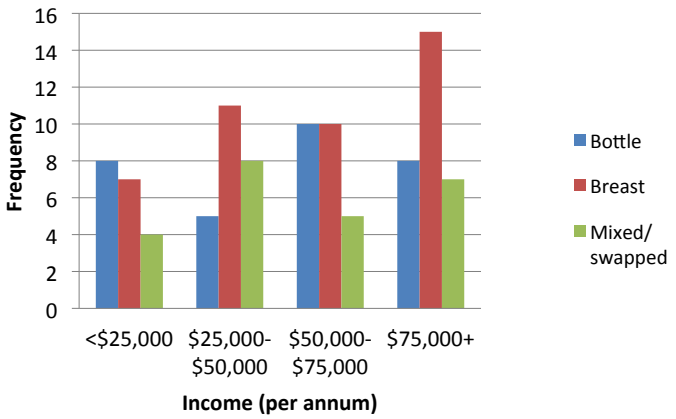

Figure 6. *A graph indicating the choice of feed in income distribution.*

The choice of the respondents' mother was associated with the respondents' choices. Of the 56 respondents who were aware of their mother's breastfeeding choice, 43% (n=24) breastfed when their mother breastfed and 25% (n=14) bottle fed when their mother bottle fed. This compared with 19.5% (n=11) who breastfed when their mother bottle fed and 12.5% (n=7) who bottle fed when their mother breastfed. These differences were statistically significant (chi square 6.595, df 1, p= 0.01) (Table 3).

Table 3. *Respondents' choices and their mothers' choices.*

		Respondents' choice	
	Total= 56	Breast	Bottle
Respondents' mothers' choice	Breast	n=24	n=7
	Bottle	n=11	n=14

Low income (<$25,000) was associated with an increased proportion of the respondents' mothers bottle feeding as compared with the highest income group ($75,000+); however, this association failed to reach statistical significance (chi square 3.796, df 1, p=0.051) (Figure 7).

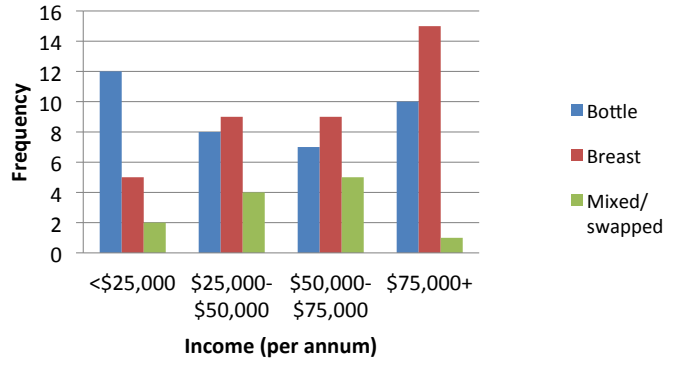

Figure 7. *A graph indicating the choice of feed by the respondents' mothers in income distribution.*

The internet was used only by those under the age of 35 for feeding information. No 18-25 year olds sought information from their family or friends and only one respondent in this age group would have liked more information. Respondents whose mothers chose to bottle feed, more frequently sought information across all sources except for family and friends; however, this did not reach statistical significance (chi square 4.53, df 5, p= 0.48) (Figure 8).

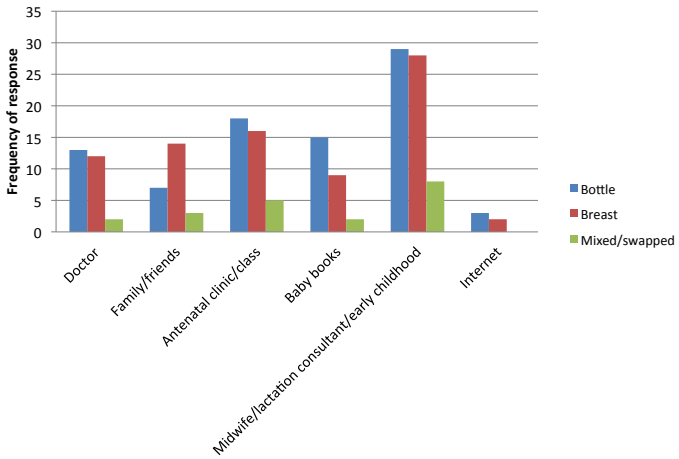

Figure 8. *A graph indicating the information sources in respondents' mothers' choice distribution.*

Discussion

Overview

This study demonstrated a number of interesting findings. Firstly, there were trends suggesting that income may be associated with the respondents' mothers' choices and the respondents' choices, with a higher proportion of respondents with the lowest incomes having mothers who bottle fed, and a higher proportion of those with the highest incomes choosing to breastfeed. These findings approached statistical significance for the income/respondents' mothers' choice association. Secondly, respondents were more likely to choose the feeding method chosen by their own mother, with these results being statistically significant. Previous research has shown breastfeeding to be positively associated with the respondent having also been breastfed. [35,36] This suggests that feeding choices are highly complex in nature, with many factors influencing attitude, choice and duration including family dynamics.

Breastfeeding initiation and cessation

Specific initiation rates were not assessed in this study; however it has been previously demonstrated that Australia appears to have a high rate of breastfeeding initiation varying from 72-92%. [35,37,38-42] Despite the typically high rate of initiation, exclusive breastfeeding rates have been shown to consistently and significantly decline thereafter. This study found that 41% had stopped breastfeeding by three months and a further 15% by six months. This is similar to global trends as studies have demonstrated 42-63% had ceased breastfeeding by three months and 23-58% at six months. [38,41-43] However, there are researched benefits to extending exclusive breastfeeding until at least six months. [44]

The most common reasons for breastfeeding and for stopping breastfeeding in this study corresponded with other study responses. Insufficient milk supply is the most commonly reported reason for stopping in the literature. [41,43,45-51] Other frequent responses in the literature included that breast milk alone did not satisfy the baby, difficulty nursing, sore nipples, that the mother felt it was the right time to stop and that she wanted help with feeding. [38,51,52]

Reasons described in the literature did seem to change at time of cessation. If stopping before three months, problems were usually associated with lactation, such as latching, sucking and not enough supply. [52] If stopping after three months, the problems were usually due to conflicts with the mother's lifestyle; however, concern about milk supply continued. [52,53] In this present study the most common reason for stopping breastfeeding was due to concern about not enough milk supply. However, two studies from developed nations demonstrated that during the early months of breastfeeding, 50% of women perceived their milk supply to be low, although their infants seemed satisfied and were not underweight. [52,54,55] Studies performed to ascertain the actual percentage of mothers with poor supply found <5% were unable to produce enough milk. This discrepancy may be due to the lack of normal lactation knowledge or technical difficulties in feeding, rather than an actual inability to produce enough milk. [52,56-59]

Bottle feeding

While there is much research surrounding breastfeeding, the needs of bottle feeding mothers should not be ignored, as 32% in this study bottle fed and 25% chose to mix or swap feed. These results were similar to the Unicef baby friendly initiative, which showed that a vast majority receive some formula milk in first year of life. [60-62] There are many different thoughts expressed by women from the literature. Some women felt breastfeeding had been romanticised in that their idealised expectations were often different from the reality of their experience. [37,63] A number of women who chose to formula feed had experienced negative emotions and a sense of failure once making the decision to bottle feed. [60] One woman in this study commented: "Because it did not come naturally to me, I felt like a failure. [This] could have led to post natal depression. There was a lot of pressure to breastfeed by midwives and nurses. It was frowned upon [when I chose] to bottle feed. I was given little support when I chose to use the bottle."

The proportion of women bottle feeding may be influenced by their beliefs. Twenty-two percent of women in this study thought that bottle feeding was as good as breastfeeding. This was comparable with 20.4% in the literature. [46]

Information and support

The most frequent source of information from this study and the literature was healthcare providers. From the previous research, 87-92% of healthcare workers involved in obstetric care talked about breastfeeding. [38] This seems to be an expected role for healthcare workers, as one woman in this study commented:

"More help needs to be given to breastfeeding mums on the maternity ward- post birth [for those experiencing problems]. Mothers should stay on the ward longer if their milk doesn't come through."

According to the literature, 90% of nursing mothers would have welcomed a midwife home visit if it had been available. [43] A review of breastfeeding strategies shows that lactating women who receive professional support breastfeed for longer than those who do not [51,64]. Factors identified in the literature that would have encouraged bottle-feeding mothers to breastfeed included more information in prenatal classes, television, magazines, books and family support. [65]

This study indicated that women were more likely to choose the type of feeding that their mother choose. From the literature, the nursing mother's mother was seen as an important source for empathy and approval and was influential to their confidence in continuing to breastfeed and in introduction of solids into the child's diet. [37,35,66,67] In this context, it is important to note that more confident women were more likely to choose breastfeeding, to persist when confronted with difficulties, to employ self-encouraging thoughts and to react positively to perceived difficulties. [41] Conversely, if a woman's mother was unsupportive, her attempts to breastfeed may have been undermined. [37,68] This influence was even more prominent for women of low income. [36] It is interesting to note that in this present study there was also a trend towards an association between the respondents' incomes and the respondents' mothers' choices. In this instance, income may be a generational indicator of social attitudes and learned behaviours rather than a direct cause of reduced breastfeeding.

Although many women experienced difficulties with breastfeeding, the literature indicates that many felt unprepared for the difficulties. [37] Breastfeeding rates might be improved upon by supporting women through these problems. One woman in this study reported:

"Women should be advised about breastfeeding problems. There is a

lot of talk about it being best for baby, but not enough about things that can affect it. This leaves you feeling [like] a failure and [this] is why I believe most people give up. If they were more prepared they may [have persisted]. As a mother who experienced difficulty with my first child, it was only through personally seeking info and determination that I was able to feed for 8.5 months."

Limitations of the study

Limitations in this study included not reaching statistical significance for some factors which appeared to have trends, such as income compared with personal choice or respondents' mothers' choice. This is possibly due to the modest sample size. As this was a cross-sectional study, it was not possible to determine causative relationships. In addition, the survey instrument had not been previously validated. There were also a number of questions which could have been better formatted; for example, it may have been helpful to stipulate if the duration of breastfeeding included mixed feeds and to qualify the age at the time of feeding choice rather than at the time of survey.

Other factors not tested in this study could be considered as positive influences for rates and duration of breastfeeding. These include feeding choice made at booking-in interview, encouragement from the baby's father or woman's mother and positive maternal breastfeeding attitudes and self efficacy. [41,51,69-76] These attitudes strongly correlated with maternal age, level of education, income and marital status. [69,71,72] This study suggests there may be intermediary factors involved and that factors such as income and the mother's influence may be markers for cultural and learned attitudes which may in turn influence choice and duration of breastfeeding.

Conclusion

In conclusion, the value of this research is in identifying factors which are associated with feeding choice in order for interventions to be targeted to those pregnant and lactating women most likely to be in need of such programs. Our study demonstrated that respondents' mothers' choices regarding infant feeding were associated with respondents' choices. In combination with other research, this suggests that an important time for intervention and education is during the antenatal period when feeding choice is often made, and when there are opportunities to address expecting mothers' beliefs. [69,75,76] It may also be important to educate the influential members in the mother's life such as her partner and her mother. It has been identified that women who make the choice to breastfeed, particularly vulnerable groups such as young mothers, those with low incomes and mothers with low confidence, need to receive ongoing support and education so that they feel confident to deal with potential feeding problems. This ideally involves home visits postnatally by a person trained to help with potential feeding problems. This research contributes to an understanding that individualised education and support across the entire pregnancy and postnatal period are likely to be key factors in influencing attitudes and choices towards whether to breastfeed or bottle feed.

Acknowledgements

I would like to acknowledge and extend my gratitude to Dr. Andrew Bonney for his encouragement, guidance and support throughout this entire project. Additionally, I appreciate the support of Dapto Medical Centre for allowing me to conduct this survey.

Conflict of interest

None declared.

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Exploring barriers to the provision of palliative care in Australia

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Palliative care provides assistance for people living with a terminal medical condition, for which the primary goal of treatment is improving quality of life. There are numerous barriers to the provision of palliative care. There is little research into barriers to the provision of palliative care and little with an Australian context. This research explores barriers to palliative care in Australia through questionnaires and interviews with stakeholders. One hundred and one questionnaires were given to South East Palliative Care (SEPC) community nursing and allied health staff, general practitioners and aged care facility staff. Five interviews were conducted with representatives from SEPC, Palliative Care Australia and two aged care facilities. Most agreed that palliative care was essential in the community, hospital and aged care setting. Four major themes were identified from interviews: 1.) Education & stigma barriers; 2.) Communication barriers; 3.) Aged care barriers; and 4.) General practice barriers. Inadequate prescriptions of pain medication were a significant issue. These themes were supported by questionnaire data, with 25.6% identifying education and 28.2% identifying resources as major barriers. Knowledge of palliative care was poor in both aged care staff and GPs, only 8.3% and 38.5% respectively answering all palliative care questions correctly, compared to 64.2% amongst SEPC staff. The study addresses a deficit in previous research, identifying barriers to palliation in aged care. The data collected has potential for further research or interventional approaches to improve the provision of palliative care for Australians.

Introduction

The World Health Organisation (WHO) defines palliative care as 'an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention of suffering... and treatment of pain and other problems – physical, psychological and spiritual.' [1]

Much of the current research into barriers to the provision of palliative care relate to psychological and spiritual issues. Research into barriers to palliative care is scarce in an Australian context. Additionally, there are deficiencies in the literature relating to the provision of palliative care in aged care facilities; a setting where many palliative patients reside. [2-5]

The provision of palliative care is impeded by barriers of varying nature. Often these barriers involve interactions between healthcare professionals, particularly General Practitioners (GPs). [2-6,10] Improvement is required in both the frequency of referrals and communication with palliative care facilities. Additionally, there is a need for increased communication and interactions between aged care facilities and palliative care providers. [2,9]

Inadequate teaching and experience of palliation in the medical profession has been seen to be a major issue, repeatedly being identified by doctors as a major contributor to an apparent lack of understanding. [3-6,10] A large proportion of doctors (72-76%)

have been found to be inexperienced in the management of pain in palliative care. [9,11] Consequently, many patients experience severe pain in the final stages of their lives. [9,12] This failure of adequate pain management may be attributable to the fears of doctors in prescribing palliative doses of analgesia, often due to anxiety surrounding physical or psychological addictions to opiates or the stigma associated with analgesia-related deaths. [9,11]

This study seeks to further investigate the barriers to the provision of palliative care in an Australian context, through cross-sectional qualitative and quantitative data collection. It aims to explore barriers relevant to the provision of community palliative care, as well as grossly assessing knowledge of palliative care in healthcare professionals and determining potential suggestions to address any identified barriers.

Methodology

The methodology aims to elicit the best understanding of the barriers to the provision of palliative care through the involvement of the following stakeholders:

- Community palliative care nursing and allied health staff from South East Palliative Care (SEPC)
- Aged care facility (ACF) carers & nursing staff
- Palliative Care Australia - the peak body for palliative care policy advocacy and implementation in Australia
- GPs.

The results were gathered using a combination of questionnaires and semi-structured interviews. The questionnaire was distributed to SEPC, aged care staff and GPs. Consent for participation was implied upon completion and return of the questionnaire. The questionnaire contained three collection methods. The first required respondents to indicate the degree to which they agreed with a given statement, using a Likert scale (strongly disagree=1, disagree=2, neutral=3, agree=4, strongly agree=5). Secondly, questions were posed to ascertain the respondent's level of knowledge surrounding palliative care. Open ended questions enabled the collection of qualitative responses, allowing respondents to elaborate on their beliefs surrounding barriers to palliative care.

Questionnaires were distributed to 30 SEPC staff, 30 aged care staff

and 41 GPs. The GPs and the aged care staff were randomly selected from an online database of Melbourne based units/practices. A computerised random number generator was used for this purpose.

The semi-structured interview was conducted with members of SEPC and aged care facilities in person and a Palliative Care Australia representative by phone. The interview aimed to explore the stakeholder's ideas surrounding barriers to palliative care, as well as their opinions on ways to reduce these barriers. Individuals who were interviewed were not given a questionnaire to fill out to avoid replication of results. The interview was conducted by two students. Questions were asked by the same student through all interviews and transcribed directly.

Questionnaires were anonymous and were numbered and filed based on response group. The results were to be compiled according to frequencies of responses, and short response questions and the semi-structured interview results were analysed for common themes using the meaning condensation method [13] for qualitative data, and compared with the literature.

Ethics approval was granted for this project by the Monash University Standing Committee on Ethics in Research involving Humans (SCERH).

Results

Interview Results

Four prominent themes regarding barriers to palliative care were elicited: 1.) Education and stigma; 2.) Communication; 3.) Barriers in aged care; and 4.) Barriers in general practice. These themes highlight more specific barriers (Table 1).

Table 1. *Major barriers to the provision of palliative care highlighted in interviews.*

Education and stigma
• Poor awareness of palliative care services • Inadequate direct education in palliative care in the medical profession • Negative connotations associated with palliative care in the community • Fear surrounding death and dying
Communication
• Poor communication between healthcare providers, especially between GPs, aged care facilities and palliative care referral services • Poor understanding of patients' cultural, language and spiritual issues surrounding death
Barriers in aged care
• Under-training of aged care facility staff, particularly carers • Lack of advanced care planning, despite regulations requiring it to be discussed • Inadequate access to appropriate pain medication
Barriers in general practice
• Inexperience in palliative medication prescription • Legal issues and confusion differentiating palliative interventions from euthanasia • Lack of exposure to palliative patients in general practice

Questionnaire Results

The questionnaire was distributed to 101 individuals. The questionnaire response rates are summarised below:

- Fourteen South East Palliative Care community nursing and allied health staff replied (46.6%)
- Thirteen general practitioners replied (31.7%)
- Twelve aged care facility carers replied (40%)
- Total response rate = 39 out of 101 (38.6%).

Table 2. *Questionnaire responses regarding attitudes to palliative care.*

"I feel comfortable discussing death and dying with people"
• Respondents generally agreed with this statement (mean = 4.2). • Three (25%) aged care respondents answered 'neutral." A further two (16.7%) did not respond to this question.
"I felt/would feel comfortable referring someone to a palliative care service"
• Respondents strongly agreed with this statement (mean = 4.6). • Four (33.3%) Aged Care staff answered "neutral."
"Referrals to palliative care services are common in my organisation/practice"
• Respondents typically strongly agreed with this statement (mean = 4.4). • Seven respondents (18%) answered "neutral."
"I believe a palliative assessment is necessary on admission to an aged care facility"
• Large variance in responses. • Many respondents agreed with this statement (mean = 4.0). • Aged care respondents agreed more strongly than the other respondent groups.
"Palliative care is "giving up" on regular treatment"
• Respondents strongly disagreed with this statement (mean = 1.6). • Four (25%) aged care respondents answered "neutral." A further two (16.7%) did not respond.
"Language and cultural differences are likely to result in poorer outcomes for palliative patients"
• Large variance in responses. • Most respondents agreed (mean = 3.6). • Nine (23.1%) respondents answered "neutral."

Table 3. *Questionnaire responses regarding knowledge of palliative care.*

"To my knowledge, palliative care is usually provided …"

• The correct response was "from diagnosis of a terminal illness."
• This question was generally well answered:
  • 26 respondents (66.7%) correctly answered this question.
  • Aged care staff answered this question best (91.7% correct).
  • Seven (53.9%) GPs answered this question correctly.
  • Eight (57.1%) SEPC staff members answered this question correctly.
  • One (7.1%) SEPC staff member and one (7.7%) GP did not answer this question.

"Palliative care ceases to exist for a patient and their family in the following time-frame…"
• The correct response according to current Victorian practice is "twelve months after death." • Eleven (78.6%) South East Palliative Care respondents identified the correct response. • No GPs or Aged Care staff answered this question correctly.
"Palliative care may involve…"
• One (8.3%) Aged Care staff member could identify the various aspects of palliative care. • Five (38.5%) GPs could identify the various aspects of palliative care. • Only nine (64.2%) SEPC staff members accurately identified all aspects of palliative care. • Two (15.4%) GPs and two aged care staff (16.7%) believed euthanasia forms apart of palliative care.

Of the 39 surveyed, 35 indicated that they had referred someone to a palliative care service. For example, in the case of SEPC, this referral often occured as an escalation of care to an inpatient specialty unit. Table 2 summarises the responses to questions regarding attitudes to palliative care. A Likert scale (strongly disagree=1, disagree=2, neutral=3, agree=4, strongly agree=5) was used to grade responses to these questions.

Table 3 summarises the levels of knowledge surrounding palliative care in the various cohorts. Questions presented several options to the respondent, requiring them to select the correct option(s).

Figure 1 shows a visual comparison of knowledge of palliative care across the different respondent groups. Notably, the number of ACF staff and GPs that were fully aware of palliative care principles highlighted a deficit in their knowledge base.

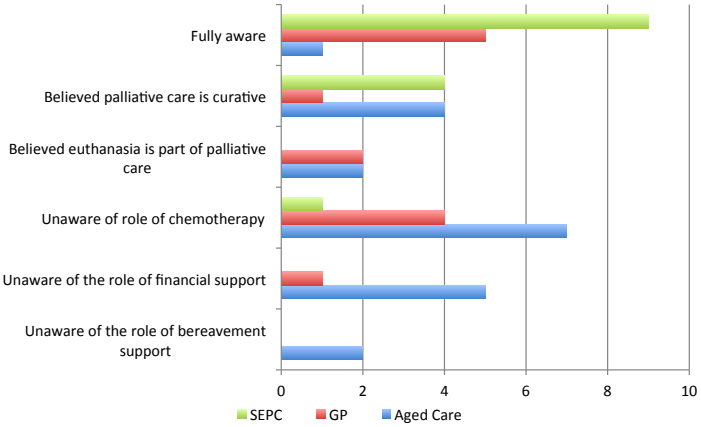

Figure 1. *Comparison of knowledge of palliative care between various respondent groups.*

Level of palliative care knowledge was directly related to frequency of specialist palliative care referrals:

- SEPC staff referred most frequently (usually weekly).
- GPs generally referred once every few months.
- Eight (66.7%) aged care staff had no experience of palliative care referrals.
    - The major reason given for not referring was that it was not the respondent's responsibility.

Summarised below are the main responses given to extended response questions (Table 4). Respondents were encouraged to describe their personal opinions on the barriers to palliative care.

Table 4. *Responses to Extended Response Questions.*

"What are some of the barriers to the provision of palliative care?"
Responses by frequency: • Lack of resources/funding (28.2%). • Poor knowledge of services by healthcare professionals (25.6%). • Poor knowledge of services by the community (20.5%). • Fear of death and "palliative" label (20.5%). • Language and cultural barriers (15.4%). • Curative focus of medicine (12.8%).
"How could these barriers be addressed?"
Responses by frequency: • Community advertising/education (30.8%). • Education and training of healthcare professionals (25.6%). • Increased palliative resources (15.4%).

Discussion

Results of both data collection methods highlight key barriers to the provision of palliative care. Both reflected the barriers previously identified within the literature. In particular, barriers relating to education, communication and GPs were consistent with previous findings. [2-4,6-10,14] The results support the evidence indicating inadequate prescribing practices in relation to pain medications. [9,11] The interview results highlighted issues surrounding aged care facilities, despite significant interventions to improve palliative care provision in the aged care sector.

Interviewees reached a consensus that palliative care is important in any healthcare setting. This information was reflected in the questionnaire results, where respondents strongly agreed that "a palliative level of care is an important part of the management of a terminally ill patient." This highlights the relevance of the topic in a healthcare context as well as the need for the barriers to palliative care to be addressed.

Most respondents felt comfortable discussing death and dying with patients. However, several respondents from the aged care cohort answered "neutral" or did not answer this question. This may highlight that the aged care respondents feel uncomfortable or may not have come into contact with this situation before.

Respondents strongly agreed that they would feel comfortable referring patients to a palliative service and did not believe that palliative care was akin to "giving up" on treatment. These results indicate that personal prejudices in the healthcare professions are unlikely to be contributing as a barrier to palliative care. Interviewees felt that these sentiments were not reflected in the wider community, which may associate palliative care with negative connotations.

Respondents strongly agreed that palliative care assessments should be an important part of the intake process of aged care facilities. Aged care staff were, understandably, most likely to agree. This question did not address whether this process is currently conducted at aged care facilities, presenting a weakness in this question. However, interviews with aged care staff highlighted that although procedures did exist for palliative assessments, these were often not implemented appropriately. Reasons suggested for this were mostly due to the family or patient's refusal, often due to unwillingness to discuss issues pertaining to their death.

Interviewees felt the main barriers to the provision of appropriate palliative care relate to a lack of awareness and education. Results from the questionnaires supported this, with many respondents believing knowledge of palliative services was poor amongst the healthcare professions, as well as the general population. This suggests a deficit in education of palliative care in healthcare training as well as the wider community. Improvements in community education programs and direct palliative education for training healthcare professionals were suggested from qualitative data collection to help to address this deficit.

The crude knowledge assessment of palliative care reflected this lack of education in the healthcare setting. Respondents from all survey groups (GPs, SEPC community nurses and aged care facility carers) indicated deficiencies in various aspects of holistic care. Whilst most respondents were able to correctly identify that palliative care is provided from the time of diagnosis of a terminal illness, only those respondents from SEPC could accurately identify that holistic palliative care may extend for twelve months after death. This deficiency is most prominently expressed in the GP and aged care staff cohorts.

A minority of the aged care and GP cohorts believed that euthanasia may form part of palliative care, which is illegal under current legislation in all jurisdictions of Australia. This could represent either a lack of knowledge about palliative care or of the definition and legal status of euthanasia. Regardless, it is imperative that healthcare professionals understand the distinct difference between palliative

care and euthanasia. As suggested previously, [9,11] it is possible that these respondents may believe that the progressive increase of pain medications, which may ultimately result in death, is a form of euthanasia. Current guidelines note that the intention of the intervention is most important. Hence, as the intention of palliative pain management is to alleviate pain and suffering, rather than death, it is not considered euthanasia.

Communication barriers highlighted an inadequacy of appropriate communication between various professional groups. Difficulties here were felt to lead to inadequate or inappropriate referrals between organisations, ultimately resulting in squandered resources and poorer patient care. Communication breakdowns between GPs and aged care staff were thought to result in inadequate access to pain medication. This suggests that these problems are due to issues surrounding poor education of aged care staff and the communication of drug orders. Improvements need to be made to ensure the GP maintains an effective role in the provision of palliative care in aged care facilities through education and improved communication and liaison.

Due to the nature of the semi-structured interview, certain limitations and a degree of bias exist in the questioning and recording of responses. In order to maintain consistency in the interviewing technique, the same interviewer was used for interviews. The recorder transcribed onto a laptop as the interview took place. This method of recording does not account for error in the documenting of discussion points by the recorder. That is, there is a potential for error as the recorder interprets the meaning of the discussion points and documents them. This was minimised due to consistency in the recorder throughout all of the interviews. The recorder's capacity was limited by their typing speed whilst maintaining intelligible notes. Whilst this may be a source of error, this was not a major issue as the recorder was able to keep pace throughout the majority of the interview. Some questions overlapped in the interviews and were covered in different areas. This could suggest that the questions could have been more generalised, or grouped better to allow for better compilation of data and minimise the time required to sort through and categorise data. Additionally, stakeholders were selected from a variety of roles in palliative care, but had a more clinical presence than bureaucratic. This may create a bias towards identifying more clinically related barriers and suppressing bureaucratic barriers through the analysis method used in this study.

It is important to note that results from both the interviews and questionnaires are only from a select few individuals. Although interview candidates were selected due to their key positions and would have a good knowledge of barriers in palliative care, it is by no means a comprehensive analysis and is from a select demographic of authoritative figures. This could potentially result in a bias towards the identification of administrative barriers rather than barriers related to actual field work. Questionnaire respondents filled this demographic and assists to eliminate some of the bias in this case. The questionnaire results, however, may not offer a proportionate representation due to the poor response rates on the questionnaire. This was further compounded by the frequency of "neutral" responses to some questions, particularly in the aged care cohort. This may indicate a lack of understanding or poor clarity of the questions. Further research should be conducted on a wider scale to ascertain a greater level of accuracy in the results.

This research would serve as a good groundwork for future research in either barriers to palliative care or more interventional approaches in order to address these barriers and improve the provision of palliative care. Specifically, suggested interventions into staff education, especially in aged care facilities, and community awareness programs were identified in the study as potential avenues for future implementation. Examples of this could be information brochures about palliative care being made available to staff and patients within the aged care facilities, integrating palliative care in training of palliative care assistants or running education seminars for aged care facility staff. Further education is vital to ensure that training healthcare professionals, particularly in the medical profession, are aware of the crucial role that palliative medicine plays.

Conclusion

Palliative care plays a critical role in the Australian healthcare system. There are many barriers which limit the effective provision of palliative care to those in need. This research investigated these barriers and identified the major issues through questionnaire and interview results from key stakeholders. Four salient themes were identified overall: communication between organisations and professionals; inadequate education of health care professionals; lack of knowledge surrounding palliative care; and insufficient pain management. Significant knowledge deficits were highlighted amongst GPs and aged care facility carers regarding palliative care. Future health promotion projects could focus on education within aged care facilities and general practice. Addressing these barriers is an integral step in furthering the effective provision of palliative care in Australia.

Acknowledgements

The authors would like to acknowledge the assistance of Dr. Robyn Cant and Ms Elizabeth Hamilton.

Conflict of interest

None declared.

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Emergency Department management and referral of self-harm patients

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Riza Gultekin is a final year medical student at the University of New South Wales. This article was inspired by his interest in emergency medicine. He plans to specialise in trauma surgery or critical care.

Aim: To outline the socio-demographic characteristics, the means of arrival, management and referral pathways for mental health presentations to the Emergency Department (ED) where the main reason for presentation is self-harm. **Methods:** A retrospective study conducted in a metropolitan hospital in Sydney. Sampled data were collected from mental health presentations to the ED for the month of May in 2005, 2006 and 2007. The data collected included patient demographics as well as management, referral and follow-up outcomes. **Results:** There were 606 patients in the sampled data (99.3% of all mental health presentations). The gender distribution of the patient cohort was 63:37 (male n=380 and female n=226) and the average age was 36 ± 16.7 years. Two hundred and three (33.5%) patients had self-harmed and 403 (66.5%) had other mental health problems. Self-harm patients' mode of arrival included ambulance (38.4%), self-presentations (36.5%), police (14%), and other. Self-harmers were mainly admitted to Psychiatric Emergency Care Centre (PECC) (28%) or discharged home (51.7%). More than one third (35.5%) of self-harm patients did not receive adequate follow-up. **Conclusion:** Important variations between self-harm patients and other mental health patients were identified in their management and referral outcomes from the ED. Clinicians need to ensure that optimal patient care is provided through appropriate follow-up of every self-harm patient post-discharge from hospital.

Introduction

Mental Health presentations to Emergency Departments (EDs) have been increasing in Australia over the last five years. [1] Mental Health presentations were defined as patients who received a psychiatric review by the emergency mental health team. In New South Wales (NSW), up to 10% of patients have stated a psychiatric complaint on presentation to the ED. [2] Self-harm (SH) is a common psychiatric presentation to the ED, especially in young people. [3]

Decision-making processes involved in the management and referral of SH patients; particularly in those with strong suicidal intent, are complex for the ED medical staff. [4] The psychiatric assessment and the consequent case referral decisions have major influences on the physical, physiological and financial outcomes of the patients, as well as on their families and the community. [5] As a result, it is crucial that decision-making processes used by the medical staff are optimal and that patients are managed appropriately according to their condition and acuity.

The purpose of this study is to outline the socio-demographic characteristics of mental health presentations to the ED and to identify the outcomes in management and referral of these presentations. The study compared the self-harm patients with other mental health presentations to the emergency department (others) and evaluated whether self-harmers were more frequently hospitalised compared with other mental health presentations.

Methods

This was a retrospective study undertaken using data collected from the ED at St Vincent's Hospital in Sydney, Australia. The hospital's large catchment area of the inner city of Sydney includes a large proportion of homeless people, residents with mental health illnesses as well as those affected by psychoactive and illegal drugs. This project was

approved by Human Research Ethics Advisory (HREA) Panels of the University of New South Wales.

The study sample includes all mental health presentations to the ED for the month of May in 2005, 2006 and 2007. In order to exclude the possible confounding factor of time of year and the likely variations in presentation characteristics associated with seasonal variation, it was decided to only sample data for the same month of each year for three years. This allowed for a large sample size. For practical reasons it was not feasible to examine all presentations for the entire three years, although this would have been ideal.

These presentations were systematically documented using the emergency department information system (EDIS™, iSOFT, Banbury, UK) as well as the medical records of the patient. The data were extracted from the medical records, coded and entered into the SPSS (SPSS Inc., Chicago, US) database. The database included patient demographics as well as information relating to management and discharge.

Four patients (n=4) were excluded due to incomplete medical records. Analysis was performed using the SPSS version 16.0 statistical analysis program. [6] Student's T-test and Pearson's Chi-Square test were used for continuous and categorical variables respectively to compare the variations between the self-harm and other mental health presentations (others) group.

Patients present to the emergency department through self-referral, referral by medical practitioners or via involuntary admission by the community mental health team or the police under a Section 22 of the Mental Health Act (2007) of New South Wales. [7] An involuntary admission to the ED requires an assessment of the patient by a doctor. From there the patient may either be released if they are deemed neither a mentally ill nor mentally disordered person, or they may subsequently be seen by another doctor if they are found to have a mental health issue.

Following examination in the ED by the psychiatric resident and discussion with the consultant, a decision is made on whether the referral pathway of the patient should be for discharge or for brief stay (24-48 hours) in the psychiatric emergency care centre (PECC), or for longer admission to an inpatient mental health centre.

The criteria for adequate follow-up consist of a documented referral

to an appropriate service following the initial presentation to ED. This may include the local or other community mental health team, drug and alcohol service, the Green Card Clinic (a specialised referral service for SH patients), the patient's General Practitioner (GP) or further in-hospital assessment with Consultation Liaison Psychiatry (CLP).

The self-harm (SH) group used in this study was defined in accordance with the WHO/EURO multi-centre study on parasuicide, in which self-harm is described as "an act with non-fatal outcome, in which an individual deliberately initiates a non-habitual behaviour that, without intervention from others, will cause self-harm, or deliberately ingests a substance in excess of the prescribed or generally recognised therapeutic dosage, and which is aimed at realising changes which the subject desired via the actual or expressed physical consequences." [8]

Results

All mental health presentations

The study population comprised 610 patients and of these four were excluded due to missing data. From the complete data available for 606 patients, the majority of the presentations were male with 380 men (62.7%) in contrast to 226 women (37.3%). The mean ± standard deviation (SD) age of the patients was 36.8 ± 16.7 years.

Of all the visits to the emergency department, 373 of the patients (61.6%) had a triage category of three. The mean length of stay (LOS) in the department was 531.4 minutes. The most frequent mode of arrival was self-presentation (39.3%) with ambulance service (30.5%) being the second most common.

The use of a Schedule 2 of the Mental Health Act (2007) for involuntary admission to the emergency department for assessment was necessary for 260 patients (42.9%) and the rest (57.1%) agreed to be assessed voluntarily. Of all mental health presentations, 61.7% required an assessment by a mental health practitioner, while the remaining patients (38.3%) only required a medical assessment by the resident.

Overall, 16.2% of all mental health presentations were admitted to the psychiatric emergency care centre (PECC), 7.9% to the in-patient mental health centre (Caritas), 5.9% to the medical ward and 2.1% to other psychiatric units. Some patients (5.6%) did not wait (DNW) for assessment and others (4.1%) discharged against medical advice (DAMA).

In terms of living arrangements, 26% of the patients were homeless which included both refuge accommodation and those living on the street. The most common pathway of referral for the majority of the patients was home (52.8%).

Almost half of (45.9%) the study group did not receive adequate follow-up after their presentation to the emergency department. Of those who received follow-up, 28% received further care from consultation liaison psychiatry, while others (10.1%) were referred to the local community mental health team.

Comparison of all mental health presentations: Self-harm vs. other

Of the total sample group of 606 patients, 203 (33.5%) had self-harmed during our study and the rest (403 patients; 66.5%) visited the emergency department for other mental health issues. There were more male presentations in both the SH group (57.1% males vs. 42.9% females) and the non-SH group (65.5% males vs. 34.5% females, where χ^2 =4.04, df= l, p= 0.05) as shown in Table 1.

For triage categories, there were a greater proportion of patients triaged as category 3 and above in the self-harm patients compared to non-self-harm group (91.7% vs. 71% respectively; χ^2 =36.50, df= 4, p<0.001) as shown in Table 1. Those patients who self-harmed also had more than twice the rate of category 1 presentations; that is, where immediate assessment was required; compared with non-self-harming patients (5.4% self-harm vs. 2.5% non-self-harm).

There was a significant variation in the average length of stay (LOS) in the emergency department between the two groups. Patients who self-harmed remained in the ED for an average of 244.1 minutes longer than those who did not. The mean LOS for the SH group was 693.7 minutes, compared with 449.6 minutes in the non-SH group (SD 675.5; t= -3.42, p<0.005).

Table 1. *Gender and Triage Category comparisons between self-harm (SH) and other mental health presentations to the emergency department.*

		SH (n=203) (%)	Other (n=403) (%)	χ^2	df	p
Gender	Male	116 (57.1)	264 (65.5)	4.04	1	0.05
	Female	87 (42.9)	139 (34.5)			
Triage Category	≥ 3	186 (91.7)	286 (71.0)	36.50	4	< 0.001
	4 & 5	17 (8.3)	117 (29.0)			

There were minor differences in the mode of arrival to the emergency department between the two groups. Arrivals via ambulance were the exception, with a higher rate of ambulance presentation in those who self-harmed than those who did not (38.4% vs. 26.6%; χ^2 =9.70, df= 4, p<0.05).

Self-harm patients were more likely to be assessed by a mental health practitioner than those who did not self-harm. Eighty five per cent of those who self-harmed required a mental health assessment, whereas only 54% of non-self-harmers were seen by a mental health practitioner (χ^2 =42.64, df= 4, p<0.001). Significant differences were also found with regard to the use of Schedule 2 of the Mental Health Act (2007). Specifically, rates of involuntary admission to the ED were higher amongst self-harmers than non-self-harmers (58.1% vs. 35.2%; χ^2 =28.81, df= 1, p<0.001).

Regarding living arrangements, no significant differences were found between the two groups, as shown in Table 2.

There was some variability in the referral pathways of the two groups, with significant differences in the proportions admitted to PECC, the inpatient mental health centre (Caritas), the medical ward and those who left before treatment commenced (see Table 2). By comparison, SH patients were more likely to be admitted to PECC (23.2% vs. 12.7%) and to the medical ward (8.4% vs. 4.7%; p= 0.001) than non-SH patients. However, a larger proportion of non-SH patients were transferred to Caritas (9.7% vs. 4.4%). Similarly, non-SH patients were more likely not to wait for treatment (7.4% vs. 2.0%; p= 0.001; χ^2 =25.82, df= 8). Other referral outcomes were relatively similar between the two groups (see Table 2).

Thirty five and a half per cent of SH patients and 51.1% of non-SH patients did not receive adequate follow-up from ED (p<0.001). Non-SH patients also had twice the rate of referrals to the Drug & Alcohol service (4.2% vs. 2.0%; p<0.001). Other notable differences between the two groups included the fact that self-harmers were more likely to be referred to Consultation Liaison Psychiatry (33.0% vs. 25.8%; p<0.001), receive better follow-up treatment through the Green Card Clinic (3.9% vs. 0.5%; p<0.001) and to have greater rates of referrals to other community mental health teams (6.9% vs. 2.2%; p<0.001; χ^2 =29.67, df= 6).

Discussion

There were significantly more male than female mental health presentations. This figure was also proportionally higher in the non-SH group where there were almost twice as many males as females. Even though Schnyder and Valach [9] have demonstrated contrary results, it is vital to recognise that the uneven male-to-female ratio of self-harm patients may be due to the fact that the hospital's location in the inner city of Sydney includes a high number of homeless males as well as a large percentage of homosexual men.

Mental health patient triage codes reflected a higher urgency distribution pattern in self-harm patients compared with that of other

Table 2. *Comparison of consultation variables, referral pathway and follow-up outcomes between self-harm (SH) and other mental health presentations to the emergency department Figures are numbers (%) of consultations.*

		SH (n=203) (%)	Other (n=403) (%)	χ^2	df	p
Mode of Arrival	Self-presented	74 (36.5)	164 (40.7)	9.70	4	0.046
	Ambulance	78 (38.4)	107 (26.6)			
	Police	30 (14.8)	77 (19.1)			
	Police & Ambulance	9 (4.4)	20 (5.0)			
	Other	12 (5.9)	35 (8.7)			
Use of Mental Health Act (2007)	Yes	118 (58.1)	142 (35.2)	28.88	1	<0.001
	No	85 (41.9)	261 (64.8)			
Seen by Mental Health Practitioner	Yes	162 (79.8)	212 (52.6)	42.26	1	<0.001
	No	41 (20.2)	191 (47.4)			
Living Arrangements	Owner/renter	132 (65.0)	242 (60.0)	5.38	4	0.251
	Homeless - refuge	33 (16.3)	67 (16.6)			
	Homeless - street	20 (9.9)	40 (9.9)			
	Backpack/hostel/hotel	6 (3.0)	8 (2.0)			
	Other/Unknown	12 (5.9)	46 (11.4)			
Referral Pathway	Home	105 (51.7)	215 (53.3)	25.82	8	0.001
	PECC	47 (23.2)	51 (12.7)			
	Caritas in-patient MH centre	9 (4.4)	39 (9.7)			
	Other psychiatry unit	2 (2.0)	9 (2.2)			
	Medical ward	17 (8.4)	19 (4.7)			
	DAMA	6 (3.0)	19 (4.7)			
	DNW	4 (2.0)	30 (7.4)			
	Died in ED	0 (0.0)	1 (0.2)			
	Other	11 (5.4)	20 (5.0)			
Follow-up	None/Unknown	72 (35.5)	206 (51.1)	29.67	6	<0.001
	Green Card Clinic	8 (3.9)	2 (0.5)			
	Local Community MH Team	23 (11.3)	38 (9.4)			
	Other Community MH Team	14 (6.9)	9 (2.2)			
	Drug & Alcohol Service	4 (2.0)	17 (4.2)			
	General Practitioner	15 (7.4)	27 (6.7)			
	Consultation Liaison Psychiatry	67 (33.0)	104 (25.8)			

mental health patients in ED. In our study, those who self-harmed were more likely to be triaged as category 3 or above and also had double the rate of category 1 presentations. This was consistent with the current guidelines on management of SH which state that a triage category of three or higher should be assigned if acute SH is suspected. [10]

The average length of stay (LOS) was significantly longer for self-harm than for non-self-harm patients who presented to the ED. The possible cause for the extended LOS for the self-harm group may be due to the limited number of mental health beds particularly in the PECC unit, considering that the majority of these patients were admitted to the PECC. Since SH involves physical injuries and overdose, this may further delay psychiatric assessments, resulting in a greater LOS in the ED.

In our analysis, we have found that the majority of the self-harm patients presented to the ED via ambulance, whereas the majority of non-self-harm patients self-presented. Similar results have been reported in other studies. [11,12] This high dependence on ambulance services for transport to the ED may place an additional burden on, and consume scarce resources of, the ambulance service.

Our findings show that psychiatric emergencies related to self-harm more frequently require assessment by mental health practitioners than those not related to self-harm. At the same time, self-harm patients have a higher rate of involuntary admission to the ED compared with other mental health patients. Over-representation of self-harmers in the group of patients involuntary admitted to hospital has also been demonstrated in other literature. [13-16] In our study, a 58.1% involuntary admission rate within the self-harm group was found. This figure was comparable to those reported in other research, which varied from 52% to 78%. [13,14]

Somewhat unexpectedly, living arrangements of both the SH and non-SH groups did not differ significantly. It was more surprising to note that in both groups the majority (65.0% in SH and 60% in non-SH) of the patients reported to live in sheltered housing; rates which are notably disproportionate to those who reported being homeless (26.2% in SH and 26.5% in non-SH). Based on past evidence, we had expected to find more self-harm patients; as well as patients with mental health presentations in general; to be homeless. [9]

The preferred referral pathway following ED assessment of patients was their usual place of residence, which was home for 51.7% of SH patients and 53.3% of non-SH patients. The most significant differences in terms of referral pathways between the self-harm group and the non-self-harm group were that a considerably higher proportion of the self-harm patients were admitted to the PECC. The aim of the PECC is

to provide medical and psychiatric care to those who experience an acute mental health crisis. The on-site availability of a 24-hours-a-day PECC at our hospital may have contributed to an increased use of this facility.

However, it may also be argued that self-harmers are typically 'acute short-term' profile patients who often only require a brief (24-48 hours) intervention via PECC to acutely manage their crisis, whereas other mental health patients may have more of a 'chronic-long-term' profile that will need longer admission within an inpatient mental health facility (Caritas). In support of this idea, a larger proportion (9.7% vs. 4.4%) of non-SH patients were transferred to the Caritas inpatient unit.

Following ED assessment a higher proportion of both SH and non-SH patients failed to receive appropriate follow-up. However, this was considerably more prominent in the non-SH group in which 51.1% of patients (compared with 35.5% in SH) had no follow-up after their visit to the ED. Suicidal behaviour including attempts, threats and ideation is a key indicator of potential suicide in the future. The first two years following the initial presentation to ED for suicidal behaviour is usually the time of most increased risk of suicide. [17] With this evidence in mind, it was particularly concerning to find such low rates of follow-up of mental health patients in our study.

Furthermore, self-harm was significantly associated with clinicians' decision to admit the patient. It was found that 33.0% of SH patients were admitted from the ED in contrast to 25.8% of other mental health patients. Higher rates of hospitalisation of mental health patients have been reported in other studies. [1,9,18] It has also been shown that when suicide is the presenting problem in ED, the clinician's notion that the patient was suicidal was strongly linked with the decision to admit, [19] which further supports our findings.

It is valuable to consider that the availability of inpatient services or outpatient alternatives often varies for each hospital and that these may influence the referral pathway decision. For instance, a complicating factor in our study was that PECC was only established in 2006; hence in the first mental health referrals from May in 2005, PECC intervention for self-harm patients was not available.

Clinicians' personal judgments, as well as the dissimilarities between patient cases, may also lead to inconsistent results since there may be differing views from one clinician to another in the assessment of the patient's exact level of suicide risk. These crucial factors may also have an important impact on referral pathways.

In order to develop a closer understanding of the differences in decision making amongst clinicians, future research needs to analyse the reasons behind the use of particular variables more than others in the management and referral of patients from emergency psychiatry. For example, other factors not used in this study such as education, employment, patients' referral pathway preferences, capacity to communicate, family support structure (i.e. presence of next of kin) and having a long-term general practitioner may also be of significance. Another significant outcome that could be measured in further studies is compliance of patients with follow-up.

Similar research methodology for studies should also be used so that clinicians from different hospitals can accurately compare the mental health presentations between the hospitals. Furthermore, dissimilarities between hospitals insofar as location, period of data sampling, population sample, availability of beds and services are concerned, need to be considered in future studies.

Conclusion

We may conclude that our typical self-harm patient in the ED was more likely to be a male, to present via ambulance with acute SH, to be triaged at category 3 or above and to have a longer stay in ED than other mental health patients. The typical patient was also more likely to be seen by a mental health practitioner, to be admitted involuntarily to PECC, to be discharged to their home or usual residence and to receive no further follow-up.

The most important recommendation that can be made from this study is that clinicians must ensure that their level of care does not end with the discharge of the patient, but that appropriate follow-up arrangements are made to ensure continuity of care within the community, as well as for the well-being and safety of self-harm patients in the long-term.

Acknowledgements

Professor Kay Wilhelm, Consultation-Liaison Psychiatry, St. Vincent's Hospital, Darlinghurst.

Dr Tad Tietze, Staff Specialist in Psychiatry at St. Vincent's Hospital, Darlinghurst.

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Conflict of interest

None declared.

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Early impact of rotavirus vaccination

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Cassie is undertaking a Masters of Public Health and Tropical Medicine in conjunction with her medical studies. This review article was written as part of a Tropical Medicine subject. She is passionate about global health and has special interests in nutrition, women's and children's health.

Background: Rotavirus is the most common cause of severe gastroenteritis in children and two vaccines to prevent rotavirus infection have been licensed since 2006. The World Health Organisation recommends the inclusion of rotavirus vaccination of infants in all national immunisation programs. **Aim:** To review current literature evaluating the global impact of rotavirus immunisation programs over the first two years of their implementation. **Methods:** A MEDLINE search was undertaken to identify relevant observational studies. **Results:** Eighteen relevant studies were identified which had been carried out in eight countries. Introduction of the vaccine was associated with a reduction in all-cause gastroenteritis hospitalisation rates of 12-78% in the target group and up to 43% in older groups ineligible for the vaccine. Hospitalisation rates for confirmed rotavirus cases ranged between 46-87% in the target group. Mortality from all-cause gastroenteritis was reduced by 41% and 45% in two countries studied. **Conclusions:** Early research evaluating rotavirus immunisation programs suggests significant decreases in diarrhoeal disease rates extending beyond the immunised group. Further monitoring will allow vaccine performance to be optimised and for the long-term effect of vaccination programs to be assessed.

Introduction

Rotavirus (RV) is the most common cause of severe diarrhoea in infants and young children. It has been reported to cause over two million hospitalisations and half a million deaths annually in children under five, with 85% of deaths occurring in low and middle income countries. [1] In recognition of the high burden of childhood morbidity and mortality, attempts to develop a vaccine against rotavirus have been underway since the early 1980s. Clinical trials of two oral vaccines in middle- and high-income countries demonstrated vaccine efficacy of 85-98% in preventing severe rotavirus gastroenteritis. [2]

The vaccines, RV1 (Rotarix - oral live-attenuated monovalent human rotavirus vaccine; Glaxo Smith Kline Biologicals, Rixensart, Belgium) and RV5 (RotaTeq - oral live human-bovine reassortment multivalent rotavirus vaccine; Merck & Co Incorporated, US) have since been licensed in over 80 countries, and national immunisation programs have commenced in several countries in the Americas, Australasia and Europe. [3] RV1 is a two-dose vaccine which the manufacturer states should be completed by the age of 24 weeks. RV5 is a three-dose vaccine which should be administered before 36 weeks. A previous vaccine, RotaShield (oral rhesus-human tetravalent reassortment vaccine; Wyeth-Ledarle, US) was licensed in 1998 but withdrawn less than a year later due to an association with intussusception.

Until recently no association had been found between either RV1 or RV5 and intussusception in clinical trials or the post-licensure period, [3] but evolving research has cast doubt on the assumption that the RV1 vaccine is entirely safe. Case-series and case-control analysis found a significantly increased risk of intussusception on days 1-7 following

the first dose of the vaccine in Mexico, but not in Brazil. However, the authors concluded that these findings were outweighed by the substantial benefits of rotavirus vaccination programs, and regulatory bodies reviewing the data have recommended that vaccination programs continue, with further monitoring of adverse events to be conducted. [4]

Despite the overwhelming need to address rotavirus rates in low income countries which bear the greatest burden of diarrhoeal disease and mortality, the World Health Organisation (WHO) initially recommended that rotavirus vaccines should only be included in national vaccination programs in countries "where data on vaccine efficacy suggest a significant public health impact." [5] There was concern that, as in the case of previous rotavirus vaccines and other oral vaccines (including polio and cholera), the vaccine may not be as effective in these settings due to a range of host and environmental factors. [6] These concerns were largely allayed by a large phase III trial of RV1 in Kenya and Malawi that found an overall efficacy of 61.2% against severe rotavirus gastroenteritis and 30.2% efficacy against severe gastroenteritis of any cause. [7] While these results were less dramatic than those demonstrated in middle- to high-income countries, they provide hope for a considerable reduction in childhood mortality related to diarrhoeal disease due to the burden of severe disease in similar settings. Studies in other low-income countries are ongoing. The WHO has since recommended the inclusion of rotavirus vaccination of infants into all national immunisation programs, with particular focus on countries where diarrhoeal deaths account for ≥10% mortality among children less than five years old. [5] The Global Alliance for Vaccines and Immunisation (GAVI) will provide financial support for eligible low-income countries to purchase rotavirus vaccines. [6]

Despite the encouraging data provided by the pre-licensure data presented above, continued research is essential to monitor the effectiveness of rotavirus vaccines in real world settings. It is not known how the vaccines will perform under routine public health use, including whether partial vaccination confers protection and whether sustained protection throughout childhood will be achieved. Other questions that remain include whether vaccination of infants will

confer herd immunity and have an indirect effect on older unvaccinated children, and how routine vaccination will impact on the epidemiology of disease including seasonality and serotype distribution. [8] The WHO has issued a policy to guide the monitoring of rotavirus vaccination programs, which advocates use of ecological methods including active surveillance systems (primary sources) or routinely collected data such as hospital discharge data (secondary sources) to assess the impact of the vaccine on the burden of disease in the population. It also suggests that a case-control design may be useful to assess vaccine effectiveness if baseline data is unavailable or if vaccine coverage is not yet high enough for ecological methods to show an impact of the intervention. [2] The first national immunisation programs were launched in 2006 and early evidence of the effectiveness and impact of RV1 and RV5 vaccines is emerging. This evidence will be analysed in this review.

The objective of this review article is to review current literature evaluating the global impact of rotavirus immunisation programs over the first two years of implementation.

Methods

A literature search was conducted using the MEDLINE database with search terms "rotavirus vaccine," "rotavirus vaccination," "RotaTeq" and "Rotarix." Reference lists of identified studies were also checked for relevant additional studies not identified by this search.

Inclusion criteria were:

- Setting: country where national rotavirus immunisation has been initiated
- Date: commencement of immunisation program preceding study period
- Methodology: ecological, surveillance or case control study
- Outcome measure: rotavirus or acute gastroenteritis (AGE) epidemiology (rates of notification, outpatient presentations, hospitalisations, mortality, laboratory results)
- Availability of English language article or translation.

Results were classified by outcome measure, country and data source, with the youngest subgroup for which data is available considered the target group as many of these children would have been eligible for vaccination. Any identified effect on older, unvaccinated age groups was also considered. Where vaccine coverage was recorded it refers to completion of the full vaccine course.

Results

Eighteen relevant studies were identified: seven conducted in the United States (US), six in Central America (Mexico, Nicaragua, Panama, El Salvador), two in Brazil, two in Australia and one in Austria. Studies were conducted between 2007 and 2010 following introduction of national immunisation programs in 2006-2007. Fifteen studies used an ecological methodology. Three were case-control studies. Ten studies were conducted where RV5 was used in local programs, seven assessed RV1 and one country used both vaccines.

The results of all studies, stratified by outcome measure, are presented in Table 1. The varying methodological methods and stage of implementation of the immunisation program prevent direct comparison of all results, so the evidence from each country is summarised below.

Table 1. *Gastroenteritis epidemiology following universal rotavirus vaccination.*

Outcome measure	% Reduction target group (age)	% Reduction in unimmunised (age)	Vaccine type, coverage rate	Study location	Study year	Data source [reference]
Mortality: AGE	41% (<1y)	29% (1-2y)	RV1, 51%	Mexico	2007	Secondary [9]
	45% (<1y)		RV1, 77%	Brazil	2008	Secondary [10]
Outpatient presentations: AGE	28% (<1y)	21% (1-4y)	RV5, 37%	Nicaragua	2007	Secondary [11]
	85% (<2y)		RV5, N/A	Houston, US	2008	Case-control [12]
	85% (<5y)		RV1, N/A	Alice Springs, Australia	2007	Case-control [13]
Hospitalisations: AGE	12% (<1y)	-5% (1-4y)	RV5, 37%	Nicaragua	2007	Secondary [11]
	37% (<5y)		RV1, 72%	Panama	2008	Secondary [14]
	40% (<2y)	36% (2-5y)	RV5, N/A	New York, US	2008	Primary [15]
	48% (<1y)	19% (1-4y)	RV1, 78%	Brazil	2007	Secondary [16]
	50% (<2y)	43% (2-3y)	RV5, 33%	US (18 states)	2008	Secondary [17]
	52% (<1y)		RV1, 74%	Mexico	2009	Primary [18]
	61% (<5y)		RV1, 61%	El Salvador	2009	Primary [19]
	78% (<5y)		RV1, N/A	Alice Springs, Australia	2007	Case-control [13]
Hospitalisations: rotavirus cases	46% (<2y)		RV5, N/A	Nicaragua	2007-08	Case-control [20]
	65% (<2y)		RV5, 75-80%	Queensland, Aus	2008	Secondary [21]
	72% (<18y)		RV5, N/A	Florida, US	2008-09	Primary [22]
	79% (<1y)		Mixed, 72%	Austria	2009	Primary [23]
	86% (<2y)	70% (2-3y)	RV5, N/A	New York, US	2008	Primary [15]
	87% (<18y)		RV5, 50%	Philadelphia, US	2007	Primary [24]
RV Notifications	65% (<2y)	56% (2-4y)	RV5, 75-80%	Queensland, Australia	2008	Secondary [21]
Proportion of positive laboratory results for rotavirus	43%		RV5, 75-80%	Queensland, Aus	2008	Secondary [21]
	58%		RV5, N/A	Florida, US	2008-09	Primary [22]
	69%		RV5, N/A	US	2007-08	Secondary [25]
	86%		RV5, N/A	US	2008-10	Secondary [26]

United States

Post-licensure surveillance began in the United States following the inclusion of RV5 in the national immunisation program in 2006. Analysis of hospital discharge information from 18 states in 2008 found a 45% reduction in AGE hospitalisations, comparable with the 59% reduction found in pre-licensure studies. [17] Similar findings emerged from active surveillance carried out in New York State, Philadelphia and Florida. [15,22,24] A case-control study in Houston found that a complete RV5 series provided 96-100% protection against severe disease requiring hospitalisation or intravenous hydration. This study also assessed partial courses, calculating vaccine effectiveness to be 69% for one dose of the vaccine and 81% for two doses. [12]

There was a 69% reduction in overall positive laboratory results for rotavirus in the 2007-8 season using national data, increasing to 86% by 2008-10. The effect of the vaccine on the seasonality of rotavirus infection was analysed in both of these studies finding that the epidemic season was delayed and substantially shorter than previous years preceding the immunisation program and that by 2009-10 it did not meet the threshold to define the start of the season. [25,26]

Australia

Australian states and territories implemented routine vaccination programs independently, which has resulted in both RV1 and RV5 being used across the country. Queensland introduced RV5 immunisation in infants in July 2007 and by 2008 rotavirus notifications in children less than two years old had declined by 65%. [21] Additionally, the proportion of positive tests had reduced by 43% as compared with 2006. [21] Significant reductions were also seen in older age groups. The Northern Territory began immunising infants with RV1 in late 2006 and a Central Australian rotavirus epidemic in 2007 provided an opportunity to evaluate vaccine effectiveness. The full vaccine course was found to be 78% protective against hospitalisation for gastroenteritis and 85% against confirmed cases of rotavirus. [13]

Central America

Mexico introduced RV1 universally in May 2007. Analysis of hospitalisation rates in 2008-9 found a 40% reduction in gastroenteritis admissions for children less than five years old, most pronounced in infants (89% of whom had been immunised). However, there was no change found among older children who were not immunised. [18] Another study found that diarrhoea-related mortality in infants was reduced by 41% and mortality in children one to two years old also decreased by 29% despite few of these children being eligible for vaccination. [9]

Nicaragua is a low-income country in Central America and was the first GAVI-eligible country to initiate universal rotavirus immunisation in 2006, with the vaccines provided by the manufacturer. Analysis of national data one year after introduction of RV5 vaccination, when 37% of infants had been immunised, demonstrated a 28% reduction in outpatient gastroenteritis presentations and 12% decline in hospitalisations for AGE in children less than one year old. A 21% reduction in outpatient presentations was also found in older children; however, there was a 5% increase in hospitalisations among children aged one to four years in 2007. [11] A case-control study in 2007-8 found vaccine effectiveness of 46% against rotavirus disease requiring admission or intravenous hydration, with stratification of severity identifying increased effectiveness against severe (58%) and very severe (77%) gastroenteritis. [20]

Panama is a middle-high income country which introduced RV1 vaccination nationally in 2006. By 2008, with 72% coverage, there was a 37% reduction in childhood gastroenteritis admissions and a blunting of the seasonal peak. [14]

El Salvador, a low-middle income country in the same region, had a reduction in rotavirus hospitalisation rates of 69% with 69% vaccine coverage. [19]

Brazil

Brazil began national immunisation with the RV5 vaccine in 2006 and assessed the impact of the program using national hospital discharge data in 2007. A 48% decline in AGE hospitalisations was found in infants, slightly greater than the findings of phase III clinical trials of the vaccine in Latin America (39%). Nineteen percent fewer hospitalisations in one to four year olds was also shown, and the greatest decline in both age groups was seen in areas of Brazil with the greatest vaccine coverage. [16] Mortality was assessed in a subsequent study which found that 45% fewer infants died of gastroenteritis in 2008 following initiation of rotavirus vaccination. [10]

Austria

Austria introduced national immunisation for rotavirus in July 2007, initially with RV5 then RV1. Sentinel surveillance found a decrease in hospitalisations for rotavirus gastroenteritis of 79% in the target population, with significant reductions seen in unimmunised children: 47% fewer cases among of children less than three months, 38% reduction among five to fifteen year olds. [23]

Discussion

These results represent the preliminary outcomes of national rotavirus immunisation programs and demonstrate real-world effectiveness of the two licensed rotavirus vaccines. Within three years of implementation, a significant reduction in the burden of diarrhoeal disease is evident among the infant population eligible to receive the vaccine. Confirmation that RV1 and RV5 provide significant protection against hospitalisation for AGE in a real-world setting suggests that substantial gains could be made in reducing the global burden of diarrhoeal disease once the vaccine is widely distributed.

Four of nine studies assessing hospitalisation relating to all-cause gastroenteritis had results comparable to the phase III clinical trials (reductions of 37-61% in the target population compared with 42-59% in the efficacy studies). Of the remaining two studies, one had much higher effectiveness (78%) as it carried out during a rotavirus epidemic; the other demonstrated a reduced impact (12%) but this was undertaken in a low-income country at a very early stage of the vaccination program when vaccine coverage was low.

Indirect effect

Several studies found a significant improvement in rotavirus rates in older, unimmunised age groups and suggested that this was an indirect effect caused by 'herd immunity,' or the overall reduction in transmission of rotavirus due to a proportion of the population being immunised. The magnitude of the effect on both populations exceeds any likely annual variation in gastroenteritis epidemiology, and together with the consistency of results across four continents, these findings suggest a significant indirect benefit to the broader population.

Countries such as the Netherlands concluded that universal rotavirus immunisation would not be cost-effective based on pre-licensure data, but recognised that the level of indirect protection is a major factor determining cost-effectiveness. [27] Therefore inclusion of this emerging data in economic modelling may influence national decision-making in regards to the need for rotavirus vaccination.

Vaccine coverage

It was not possible to compare the relationship between any outcome measures and vaccine coverage rates, as few studies were able to provide an accurate coverage rate during the early phases of the immunisation program. In the US there is an extensive lag time between vaccination and public reporting. Furthermore, the multi-dose regimens (two doses for RV1 and three doses for RV5;)complicate the reporting and comparison of immunisation status in other countries. [17] However, the magnitude of improvement in rotavirus rates in studies where vaccine coverage was likely to be low suggests that a degree of protection from partial vaccination may be occurring. This is particularly relevant in developing countries where up to one-third of

the burden of severe disease occurs in infants under six months who are not fully vaccinated. Further research is required to address the role of partial vaccination. [20]

Rotavirus season

The impact of the vaccination program on seasonality of rotavirus disease was found in several studies, with blunting of the seasonal pattern seen. In some cases such as Mexico in 2008-9, there was no apparent 'season' at all. Changes in these epidemiological patterns demonstrate an appreciable impact on the previously predictable rotavirus pattern in temperate areas throughout winter and spring.

Vaccine strains

None of the studies were able to assess whether introduction of the vaccine had led to alteration in the prevalent circulating strains of rotavirus; however, this will need to be evaluated in the longer term as the effectiveness of current vaccines may be affected by serotype replacement. The considerable variability in study methods prevented comparison of the impact of the two vaccines RV1 and RV5. A Cochrane review recommended new trials be conducted with head-to-head comparison of the two vaccine types. [3]

Developing countries

A major concern following the pre-licensure clinical trials, largely conducted in middle- to high- income countries, was whether the vaccine would be as effective in developing countries, where 85% of deaths from diarrhoeal disease occur. Trials in Africa demonstrated significant improvement in rates of diarrhoeal disease, though not as impressive as those in the original trials. [7] The post-licensure monitoring data reviewed in this study similarly shows that while rotavirus vaccination has led to improvements in diarrhoeal disease in Central and South American countries, the improvement is to a lesser degree than in developed countries. Successful integration of rotavirus into Nicaragua's childhood immunisation program and achievement of >80% vaccine coverage provides an encouraging precedent for other developing countries to introduce the vaccine. [11,20] Another review has assessed the impact of the vaccine in both developing and developed countries with similar conclusions: while vaccination programs appear to be less effective in impoverished populations, there is a greater absolute reduction in severe disease and significant improvement in public health can be expected where universal rotavirus vaccination is introduced. [28]

Study limitations

There are several limitations of the observational and ecological studies included in this review which will be briefly discussed. Studies based on secondary data sources have the potential to introduce bias because private hospitals or laboratories were not included in government data collection and there may have been interhospital differences in practices to test for rotavirus, admit patients or classify cases. Use of sentinel hospitals does not capture the entire target population; however in most cases they have been designed to cover the majority of the target population (for example, paediatric referral hospitals). All studies suggested a positive impact from the vaccination programs; however without access to unpublished data it is difficult to determine whether publication bias has contributed to this finding.

Many studies used all-cause gastroenteritis as a surrogate for rotavirus disease, with rotavirus known to cause 30-50% of all AGE hospitalisations in children. [2] However this methodology does not control for variability in the circulation of other gastroenteritis causing pathogens, or trends in other factors influencing diarrhoeal disease such as sanitation, water or nutrition.

While study limitations mean that it is not possible to definitively conclude that rotavirus immunisation was responsible for the decline in gastroenteritis rates, the dramatic change following introduction of immunisation in eight countries, as analysed in this study, provides strong evidence that rotavirus vaccination programs are having an appreciable impact on the burden of diarrhoeal diseases.

Future monitoring

Many of the studies utilised routinely collected data for which historical information was available for comparison as this method has minimal additional costs. However, broader use of active surveillance is important to accurately evaluate the impact of vaccine programs and potentially to identify ways to improve the effectiveness of the program to have the greatest impact on the morbidity and mortality of diarrhoeal disease. [29]

Conclusions

National rotavirus immunisation programs have been initiated in several countries since two vaccines were licensed for use in 2006. Research has emerged from eight countries evaluating the impact of the first two years of these programs in a real world setting. All studies found improvements in outcomes of diarrhoeal disease in the target population, with the greatest protection found against severe rotavirus gastroenteritis. A significant indirect effect was also detected in the unvaccinated population in some studies, which may improve the cost effectiveness of vaccination programs. Active surveillance methods are recommended to monitor the impact of rotavirus vaccination programs; however routinely collected data can provide useful information in resource-poor settings. Further research is required to establish the effectiveness of partial vaccination and the effect of vaccination programs on circulating rotavirus strains.

Conflict of interest

None declared.

Acknowledgements

Nicolas Smoll for his advice on writing for a publication. Henry Yu for proof-reading the article.

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The John Flynn Placement and Bonded Support Programs, managed by ACRRM, are Australian Government initiatives funded by DoHA

Balance and gait stability following sports-related concussion

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Background: Concussion is an injury that is associated with many sports, in particular ice hockey, martial arts and the various codes of football. Concussion alters the stability of a person and as stability is vital when playing sports, the consequences of undiagnosed and untreated concussions are enormous. **Aim:** To look at various methods used to assess posture and stability in athletes, and their use in making safe return to play decisions after a sport-induced concussion. **Methods:** A search was conducted through PubMed, using the terms 'concussion' and 'sport.' Article titles were initially screened by the author and if the title seemed to be relevant to the purpose of the review, the abstract of the article was then screened for relevance. **Results:** Concussion negatively impacts upon an athlete's cognitive and motor functioning. Cognitive testing has previously been assessed and is currently used; however it has been shown that cognitive function may return before motor functioning. The time taken to recover the motor component is usually between three to ten days; however, this varies considerably between athletes. Balance and gait testing are a means of objectively assessing the stability of an athlete and have proved to be particularly useful in monitoring the recovery of an athlete after suffering concussion. **Conclusion:** Balance and gait testing are means of objectively assessing the stability of an athlete. Although their use is applicable to many situations, they have proved to be of particular usefulness in monitoring the recovery of an athlete after suffering concussion. Through their use, the subjectivity of the assessment is being eliminated, ensuring informed and supported decision-making regarding the safe return to play.

Introduction

Concussion is an injury that is associated with many sports, in particular boxing, football, ice hockey and martial arts. [1] According to Powell, [1] concussion is a 'trauma-induced alteration in mental status that may or may not involve a loss of consciousness.' Tommasone and Valovich McLeod [2] state that concussion is 'a mild brain injury resulting from a direct blow to the head resulting in physiological changes in brain function.' Guskiewicz *et al.* [3] defined concussion as 'an injury to the brain caused by a sudden acceleration or deceleration of the head that resulted in immediate, but temporary, alteration in brain functions, such as loss of consciousness, blurred vision, dizziness, amnesia or memory impairment.'

Various authors have stated that concussion causes a complex cascade of ionic, metabolic and physiological events that may adversely affect cerebral function for several days to weeks. [4,5] This leads to mitochondrial dysfunction, diminished cerebral glucose metabolism, reduced cerebral blood flow and altered neurotransmission, and ultimately results in the clinical presentation of neurological deficits, cognitive impairment and somatic symptoms. [5]

It has been shown that neuroimaging, such as computed tomography (CT) and magnetic resonance imaging (MRI), is often of little use in assessing less severe head injuries such as cerebral concussion, as such injuries tend to be functional rather than structural. [6]

Importance

Recently there has been increased awareness surrounding concussion and its associated negative effects due to the media coverage of several

high-profile athletes who have attributed their retirement to repetitive concussions. [1,7] After one traumatic brain injury, the risk of a second is three times greater, and after the second injury the risk of a third increases by a factor of eight. [8,9]

One of the most challenging issues facing practitioners when dealing with concussion is making the initial diagnosis. [1,10,11] The signs and symptoms present can differ considerably between individuals. [1] A survey conducted by Ferrara *et al.* [12] found that 33.0% of athletic trainers rely upon clinical examination and 15.3% on a symptom checklist in their evaluation of concussion. Additionally, 83.5% of those surveyed stated that the use of a standardised method of concussion assessment provided more information than routine clinical and physical examination alone. [12]

The possible consequences following a concussion are serious and potentially fatal. [13] Cantu [10] discusses the Second Impact Syndrome (SIS), which occurs when an athlete who has sustained an initial head injury, most often a concussion, sustains a second head injury before symptoms associated with the first have completely resolved. It is believed that this can cause cerebral oedema leading to herniation of the brain, ultimately proving to be fatal. [10] Other consequences of concussion, such as other head or bodily injuries, may be the result of having a slow reaction time and instability.

It is critical that functional and cognitive impairment are properly identified to prevent the risk of re-injury and to minimise further complications. [14] The rate of recovery is highly individual and as a result there is no standard guideline to use when determining when a person is fit to return to play. [5,14] At present it is through the use of cognitive testing and highly subjective motor control assessment that these important return to play decisions are being made.

Methods used to assess deficit

Neuropsychological testing is a common method used to assess when a person's cognitive function has returned to pre-concussion levels. A widely used and validated test of cognitive function is the Digit Substitution Symbol Test. [15] Other commonly used tests are the Hopkins Verbal Learning Test and the Stroop Test. [3,15-16] Randolph *et al.*, [18] in investigating the use of neuropsychological testing in the management of sport-related concussion, concluded that although the theoretic rationale for use of such tests is sound, they lack sensitivity and do not meet the necessary criteria to support a clinical application. [18] Although shown to be of value in concussion evaluation, they should not be used as the sole basis of a return to play decision. [19]

There is evidence that the return of motor function is independent of the return of cognitive function and tests of motor function take a longer time to return to normal after a concussion, than cognitive tests. [20,21] It has also been found that injured athletes do not display significantly poorer performance than uninjured controls on any of the neuropsychological tests, suggesting that the tests used are not sensitive enough to reveal cognitive deficits. [16] This was further demonstrated in a later study by Guskiewicz which concluded that differences in the neurocognitive scores between injured subjects and uninjured controls did not differ as significantly as differences in balance. [22] Despite this, neuropsychological testing is being used to determine recovery after a concussion and many important decisions surrounding return to play are being made based upon this information.

At present the only methods of determining the return of motor control are subjective, relying primarily on the discretion of the practitioner. Physical signs of concussion include poor coordination, gait unsteadiness and loss of balance. [19] Numerous studies have investigated possible methods of objectively assessing the return of motor control by looking at gait and stability. [3,5,8,9,14,16,17,20,21-27] The rationale behind the use of such testing is that the areas of the brain which are disrupted as a result of concussion are those that are responsible for the maintenance of postural equilibrium. [3]

Stability is the ability to maintain a desired postural orientation in response to perturbations generated from either internal or external sources. [26] Balance is the process of maintaining the center of gravity (COG) within the body's base of support. [20] Postural instability has been identified in various pathologic conditions such as traumatic brain injury, craniocerebral injury and cerebellar atrophy. [20] It is believed that communication between the visual, somatosensory and vestibular systems is lost in the majority of these individuals, causing moderate-to-severe postural instability in either the anterior–posterior direction, medial–lateral direction or both. [20]

Concussed individuals have been shown to adopt a more conservative gait strategy to maintain stability. [14,25] It has been found that stride length decreases and stride rate increases when stability is impaired. [8,21,24] Furthermore, sway from the centre of mass, in the medial-lateral direction, is increased after a concussion. [23-25]

The research methods previously used have been complex and in a laboratory setting, generally with the use of camera analysis systems and force plates which measure the ground reaction forces. [23-27] Although these methods are effective in assessing the balance deficit they are impractical for use during game play. It is essential that testing be conducted immediately after injury to increase the accuracy with which the practitioner can assess concussion in the acute phase. [11] As yet no valid and reliable field-based procedure has been presented to quantify the deficits of concussion on motor performance.

Many studies have further investigated the assessment of postural control by introducing challenges. Altered visual cues, obstacles and divided attention are the most common methods. [13,17,24]

It has been hypothesised that by removing visual cues, the balance deficit is increased. [17] Guskiewicz *et al.* [3] believe that the overall postural stability deficit can best be explained by a sensory interaction problem. They state that this inability prevents concussed athletes from accurately using and exchanging sensory information from the visual, vestibular and somatosensory systems. [3,22] As the integration of this information is essential for the maintenance of equilibrium, postural instability is seen in concussed athletes. They found that postural instability was greatest during difficult visual conditions, or when vision was removed altogether. [3]

With the introduction of an obstacle it was found that in concussed individuals a greater postural sway was seen, the peak sway velocities were faster and the time taken to complete a stride was also significantly greater. [13,25] Chou *et al.* [8] found that the walking speed for all subjects decreased with the introduction of an obstacle; however, no differences were seen between the concussed and normal groups.

Divided attention is achieved through dual tasking. Concussed individuals display signs of instability when attention is divided. [24,25] Catena *et al.* [25] concluded that this task was most sensitive in distinguishing between the injured and uninjured controls. The subjects are asked to perform a walking or standing task whilst simultaneously undertaking other activities. Van Donkelaar *et al.* [13] found that an individual suffering from a concussion may appear normal when attempting activities in isolation yet display noticeable deficits when performing two or more tasks simultaneously. Responding to questions, performing mental tasks (such as counting down from 100 in multiples of seven) and responding to noises by pressing a handheld trigger are examples of dual tasks.

Some researchers have found that the range of motion in the medio-lateral direction in the concussed subjects was greater during dual tasking when compared to the control group. [14,24] This was further supported by a later study conducted by Parker *et al.* [21] which found that injured subjects had greater sway and sway velocity than controls when their attention was divided through the performance of simple mental tasks. Stride patterns were also found to be significantly different in the concussed groups, with an increase in the time taken to complete a stride. [25]

As a means of determining variations in postural control some studies used baselines which were obtained at the beginning of the season, prior to injury. [3,17,28] This enabled comparisons to be made on an individual basis and allowed for variations within the population. Other studies were done retrospectively with the balance deficit being monitored until it returned back to what was believed to be normal. [26] Most studies did this with the use of matched controls. [21-25]

Duration of deficit after a concussion

The time taken for balance deficits to return to pre-injury levels is one that is debated. Most studies have concluded that a concussed athlete has returned to normal within three to ten days post injury. [22,26,27]. Parker *et al.* [21] found that even athletes suffering from a mild head injury, such as concussion, had several aspects of gait stability compromised for up to four weeks after the injury. To determine this, the investigators tested athletes usually within 24 hours of injury, again on day two or three and on at least one other occasion within the next two weeks [17,22,27]. The most significant alterations in gait and stability have been found in the first three days after concussion. For athletes that have a suffered a more severe head trauma the time taken to return to normal is greatly extended, with balance deficits still being seen at least two years later. [8,9,13]

Conclusion

Balance and gait testing are means of objectively assessing the stability of an athlete. Although their use is applicable to many situations, they have proved to be of particular usefulness in monitoring the recovery of an athlete after suffering concussion. Through their use, the subjectivity of the assessment is being eliminated, ensuring informed and supported decision-making regarding the safe return to play.

Recommendations

Concussion needs to be diagnosed, and recognised as an injury with potentially severe consequences.

- As response and recovery times are largely individual, sport participants should be assessed pre-season so as to obtain baseline data and at random times throughout the playing season.
- Sport participants should undergo thorough testing after suffering a concussion to assist in appropriate diagnosis and assessment of severity.
- Although clinical examination has an important role, it should be used as an adjunct to a more objective assessment.
- Return to play should not occur until a patient no longer has a deficit, as the risk of re-injury is significant.

Acknowledgements

This publication is a modification of a section from an Honours project in which Ms Patti Denham-Mason was the primary supervisor. Dr Warren McDonald acted as a secondary supervisor, and further assisted in the recruitment of subjects for data collection.

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Conflict of interest

None declared.

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Acute blood loss in children

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Hypovolaemia is the leading cause of circulatory failure in children. Effective fluid resuscitation is a mainstay of patient management and is dependent on accurate detection of blood loss or volume depletion. Calculation of blood volume in children is based on age, weight and clinical physiology and the estimation of the volume of blood lost requires interpretation of the history and orthostatic vital signs, especially heart rates. Administration of fluids following these calculations will also be discussed.

Introduction

The accurate and prompt assessment of children presenting to the hospital emergency department with haemorrhage is critical in determining the course of their clinical care and prognosis. In this setting, circulatory shock is a major cause of morbidity and mortality. [1] Hypovolaemia is the leading cause of circulatory failure in children. [2] Early and effective fluid resuscitation is a mainstay of patient management and is dependent on accurate detection of blood loss or volume depletion. While this is vital in hypovolaemic shock, it is preferable to detect changes in blood volume before clinical shock occurs. Here, methods for estimating children's blood volume, blood loss and methods for fluid resuscitation and maintenance will be discussed.

When referring to hypovolaemia it is important to distinguish between its respective components: volume depletion and dehydration. Volume depletion refers to a loss of volume from the extracellular space (intravascular and interstitial fluid). This can occur with diarrhoea, diuresis, gastrointestinal haemorrhage and vomiting. Dehydration describes a loss of intracellular water which elevates plasma sodium concentration and osmolality. [3]

Estimating fluid compartments

In adults, total body water comprises two thirds of body mass. Of this water, two thirds are in the intracellular space and one third is in the extracellular space.[4] Thus, a 70kg adult holds 45L of water with 30L of intracellular fluid and 15L of extracellular fluid. The extracellular fluid is further divided into 10L in the interstitial space and 5L intravascularly. Total blood volume circulating in the body is 7% of ideal body weight in adults. [5] There is a third space, also referred to as transcellular fluid. It is formed from the extracellular space and contains the cerebrospinal fluid, urine, fluid in the gut, fluid in ducts such as lymphatics and serous cavities.

Fluid distribution varies between age groups. Total body water of newborn infants is 75-80% of body weight, falling to 65-70% in one-to-twelve year olds and to adult levels of 55-60% after puberty. [6] Total blood volume (TBV) circulating is 7-9% in children, depending on age. [5] The following ranges can be used to estimate total blood volume in children: premature infants 89-105mL/kg, term newborns 82-86mL/kg and infants and preschool-aged children 73-82mL/kg. [7]

Estimating blood loss

Hypovolaemic shock

Hypovolaemic shock presents with tachypnoea, tachycardia, confusion, thready peripheral pulses, cool extremities, oliguria and hypotension. [8] It occurs as a result of loss of intravascular volume from blood, plasma (in burns or nephrotic syndrome), water and electrolytes (lost in diarrhoea, vomiting and diabetes). [8] Children

will initially compensate for shock by increasing heart rate to maintain cardiac output, and tachycardia is often the first measurable sign. [9] Uncompensated haemorrhagic shock leads to hypotension due to acute decrease in venous return [10] and thus in cardiac output. Depression of blood pressure reduces the carotid sinus baroreceptor inhibition of sympathetic activation to the cardiovascular system. This central compensatory mechanism leads to increased total peripheral vascular resistance, increased venous return and increased heart rate and contractility. [5,11] This range of sympathetic reflexes can maintain arterial pressure effectively for relatively large volume losses, even more so in infants and children in whom hypotension is a very late sign.

In addition to the sympathetic reflexes, compensatory mechanisms that restore blood volume include activation of the renin-angiotensin system and release of antidiuretic hormone. These cause arteriolar vasoconstriction as well as tubular sodium and chloride reabsorption which promote renal conservation of water and salt. [5] Finally, a shift of fluid from the interstitium to the intravascular space occurs which restores volume over a longer timeframe. [12]

Uncompensated hypovolaemic shock is a critical condition and evaluating acute blood loss prior to its onset can improve medical treatment. This can prove difficult since many clinical tests for blood loss are not well-proven or tested in large high-powered studies, particularly in paediatrics.

Techniques for measuring acute hypovolaemia

The clinical assessment of hypovolaemic shock in children can be difficult. Studies looking at objective measures are largely adult-based and volume depletion and physiological responses to hypovolaemia can be quite different in children. Large reviews of clinical studies in hypovolaemia have summarised evidence for the variety of clinical signs of blood or fluid loss. The most useful signs are severe postural dizziness or postural pulse increase of 30 beats per minute or more. Supine hypotension and tachycardia, which are frequently absent, carry a high specificity when present. Dry mucous membranes and a dry axilla have a low sensitivity but reliably high specificity. [19]

If the child is lucid or has a guardian present, often the simplest method of gauging blood and fluid loss is by enquiring about the mechanism and history of the injury. Additionally, whether the child was restrained and how, whether there was any loss of consciousness and whether the wound was weeping or gushing can assist the clinician in initial volume estimates. Other helpful questions include: when did s/he last keep something down? How many wet nappies has s/he had in the last

24 hours (infants aged up to 12 months will empty their bladder on average once an hour, decreasing to about ten times per day at three years) [13-15] and what was his/her weight at the last baby check?

Capillary refill

As a quick, easily obtained and non-invasive test, the capillary refill test on the sternum has gained popularity in clinical practice as part of the Trauma Score. It is generally advised that a refill time of two seconds or more is abnormal, despite a paucity of evidence. In the paediatric setting, Schriger and Baraff [16] tested healthy participants between two weeks and twelve years of age and demonstrated an upper limit of normal of 1.9 seconds, which confirms the accepted normal value. [17] Despite this, it is worth noting that in experiments on adults the sensitivity of the capillary refill test in patients with a history of hypovolaemia and abnormal orthostatic vital signs is 26%, and 46% in ED patients with frank hypotension. [18]

Fluid resuscitation

The first step in treatment of hypovolaemia and hypovolaemic shock is adequate fluid resuscitation with either a crystalloid or a colloid solution. [20] As previously mentioned, the emergency criteria for volume administration include orthostatic tachycardia, reduced urine output, hypotension and metabolic acidosis. These signs can be very late and initial resuscitation can easily be based on history alone.

The differences between crystalloid and colloid lie in their effects on the Starling equation, which describes fluid movement between intravascular and interstitial spaces. Starling stated that the rate of fluid movement into or out of a capillary depends on the net hydrostatic pressure minus the net colloid osmotic pressure. [21] While colloids are widely used in Europe for volume replacement, crystalloids are popular in the United States. [22] The merits of either are disputed [23,24] and will be discussed below.

Crystalloids can be considered in two groups: those that contain electrolytes in similar concentration to plasma (isotonic) and those that contain lower concentrations or no electrolytes (hypotonic) but contain glucose so that their osmolality matches that of plasma (see Table 1). Only isotonic crystalloids are used in the initial management of haemorrhagic shock. On administration they are redistributed into various body fluid compartments. After fifteen to thirty minutes only 25-30% of volume remains in the intravascular compartment. [4] This is particularly true of 5% glucose, of which less than 10% remains in the intravascular compartment after the glucose is metabolised. Hypertonic saline solution can range from 1.8% NaCl to 7.5% NaCl, the latter of which can expand intravascular volume by up to 1.5 litres in boluses of 250mL.

Table 1. *The relative compositions of crystalloid solutions. Glucose-containing solutions are used to treat dehydration as a result of water loss.*

Crystalloid	Na^+	K^+	Ca^{2+}	Cl^-	HCO_3^-	pH	Osmolality
Harmtmann's (isotonic)	131	5	4	112*	29	6.5	281
0.9% NaCl	154			154*		5.5	300
4% glucose + 0.18% NaCl	31			31		4.5	284
5% glucose						4.1	278
Hypertonic saline (1.8-7.5% NaCl)	Expand intravascular volume						

** Greater than plasma concentrations.*

Colloid solutions are made up of high molecular weight particles derived from gelatin (Haemaccel®, Gelofusine®), protein (albumin) or starch (HAES-steril®) and are rarely used in the initial emergency management of haemorrhagic shock. Colloids can be given in a similar volume to the estimated deficit (Table 2). [4] While albumin persists in the body for 20 days, its duration of action within the intravascular compartment varies from less than two hours to more than a day. Gelatins produce an intravascular volume expansion effect almost equivalent to albumin, with a duration of three to four hours. [22] There is no limit to volume which can be administered, provided haemoglobin levels are maintained.

Table 2. *The relative compositions of colloid solutions.*

Colloid	Avg MW	Na^+	K^+	Ca^{2+}	Cl^-	HCO_3^-	pH	Osmolality
Haemaccel	35	145	5	6.2	145		7.3	350
Gelofusine	35	154	0.4	0.4	125		7.4	465
Albumin	69	130-160	2		120		6.7-7.3	270-300
Starch	140-400	154			154		5.5	310

Unfortunately, colloids have been associated with a variety of adverse effects including anaphylactic reactions, risks of infection with albumin, and interference with accuracy of laboratory investigations. [25,26]

Evidence for their use

While physiological explanations for colloid superiority over crystalloids have been postulated, evidence does not support their superiority. [27] In a randomised controlled trial, So and colleagues [28] found isotonic saline to be as effective as 5% albumin in treating hypotension in preterm neonates. In older children, there are limited numbers of large randomised controlled trials on fluid management of acute blood loss. Paediatric care is largely based on the results of adult trials, where the evidence supports both solutions. Velanovich [29] conducted a meta-analysis in adults and found a 5.7% relative difference in mortality in favour of crystalloids. When data was pooled into studies using trauma or non-trauma patients, the overall treatment effect was better in crystalloids and colloids respectively. In comparison, a recent SAFE Study in Australia and New Zealand compared 4% albumin to isotonic saline for intravascular fluid resuscitation in 7,000 adult intensive care patients. The relative mortality risk for patients receiving albumin compared to saline was 0.99 (95% CI, 0.91-1.09), indicating similar survival for both treatments. [30]

Paediatric data in other forms of shock confirm the lack of supportive evidence for added benefit to resuscitation with either crystalloid or colloid solutions. Two trials in dengue shock syndrome demonstrated no clear benefits between dextran 70, 3% gelatin, Hartmann's solution and isotonic saline in pulse pressure recovery time or "any complication" of fluid therapy, although six children had allergic reactions after colloids. [31] The second study in moderately severe shock comparing Hartmann's solution, dextran 70 and 6% hydroxyethyl starch found a slightly increased risk of requirement for rescue colloid in Hartmann's solution. [32] As crystalloids are significantly cheaper and show no demonstrable benefit, the clinically rational approach to resuscitation following blood loss is resuscitation with a crystalloid solution.

Finally, blood and blood components can be used in fluid resuscitation and are a mainstay of acute blood loss therapy. Packed red blood cells are used in preference to whole blood because they consist of red cell concentrate with saline, adenine and mannitol which improves red cell survival and flow. Additionally, each unit contains the same red cell mass as one unit of whole blood at around half the volume and twice the haematocrit (50-70%) and raises an adult haemoglobin by 10g/L. [4,5] Transfusion of packed red blood cells is indicated for improving oxygen-carrying capacity and increasing blood volume. The decision to transfuse is based on responsiveness to two 20mL/kg boluses of crystalloid and is indicated to maintain appropriate end-organ perfusion. In the context of trauma and acute blood loss, haemoglobin levels are not used as a guide for when to use blood.

Fresh frozen plasma (FFP) is extracted from donated blood and one unit

(200-250mL) is from a single donation. [4] It contains normal levels of clotting factors and is used to correct clotting factor abnormalities which can occur secondary to large transfusion and dilution of a patient's own factors, especially Factor VIII and fibrinogen. Cryoprecipitate is formed from thawed FFP, which is centrifuged to remove plasma and hence contains high concentrations of FVIII and fibrinogen in a small volume. This reduced volume (15mL) allows more rapid replacement of these factors than a single unit of FFP (200mL), while reducing the risk of volume overload, which is important in a small-volume patient. [33]

Volume and rate of administration

Children have a larger surface area-to-volume ratio than adults and assuming a healthy cardiovascular system can tolerate larger volumes per kilogram of weight. [34] Current World Health Organisation guidelines instruct two boluses of 20mL/kg of Hartmann's solution or normal saline in hypovolaemic shock. They recommend a third bolus if no improvement (defined as "warmer hands, pulse slows and capillary return faster") before infusing 20mL/kg blood over 30 minutes. This differs from standard paediatric practice in developed countries that follow Australian Resuscitation Council and Australian Paediatric Life Support guidelines to deliver two boluses followed by blood transfusion.

There is scant evidence in children with hypovolaemia not due to septic shock about optimal volume to be used and the velocity of fluid delivery. Efficacy of fluid resuscitation depends on the compliance of the interstitial space, existing microvascular pressures and the permeability of the microvascular barrier. [20] The best two indicators of correct fluid intake are urine output and osmolarity. [35]

Conclusion

Acute blood loss in children can be a critical presentation in emergency departments. The management of these patients and prevention of their progression to hypovolaemic shock involves three major processes: the calculation of their blood volume, which depends on age and weight and clinical acumen; estimation of the volume of blood lost using a clinical history; and orthostatic vital signs, especially heart rate and administration of fluids. The differences in paediatric physiology demand extra attention and require different approaches in medical care.

Conflict of interest

None declared.

Acknowledgements

Peter Armstrong, for his invaluable assistance in proof-reading this article.

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Management of infertility in the setting of polycystic ovary syndrome

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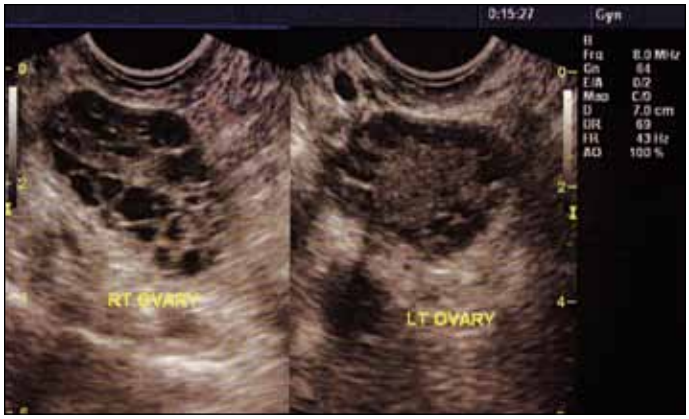
Polycystic ovary syndrome (PCOS) is a common endocrine disorder which affects a significant number of premenopausal women in Australia. PCOS has long-term clinical implications which can lead to decreased quality of life and psychological morbidity. A major contributing factor to this is the impact of PCOS on a woman's fertility. However, there are a number of treatment modalities that may be used to treat PCOS-related infertility and with appropriate treatment, a woman's prognosis with regards to PCOS-related infertility can be excellent.

Introduction

Polycystic ovary syndrome (PCOS) is a syndrome of ovarian dysfunction, hyperandrogenism and polycystic ovary morphology. [1] It is the commonest endocrine disorder among women of reproductive age and is thought to affect 5-10% of women in Australia. [2] Indigenous women are affected at a higher rate of 21%. [3] PCOS has significant reproductive implications for women including anovulatory infertility, miscarriage and pregnancy-related complications. [4] Furthermore, the state of unopposed oestrogen arising from chronic anovulation increases the risk of developing endometrial hyperplasia and cancer. [5] The exact pathophysiology of PCOS remains unknown but an underlying genetic predisposition has been suggested. Women with this predisposition are thought to go on to develop the condition in the presence of insulin resistance, which in turn can be related to the amount of adipose tissue present (Figure 1). [5]



A MEDLINE search was conducted using the key words "PCOS" and "infertility" to find the various treatment modalities currently used to treat PCOS-related infertility. The search was then restricted to English language, peer-reviewed, full text documents. The Cochrane Library was also searched using the search term "PCOS" and several articles were found following citations in other documents. This review summarises the current literature on treatment options for PCOS-related infertility, including lifestyle modification, medical therapy, laparoscopic ovarian drilling and in-vitro fertilization (IVF).

Lifestyle modification

Obesity is strongly associated with PCOS and affects 50% of PCOS

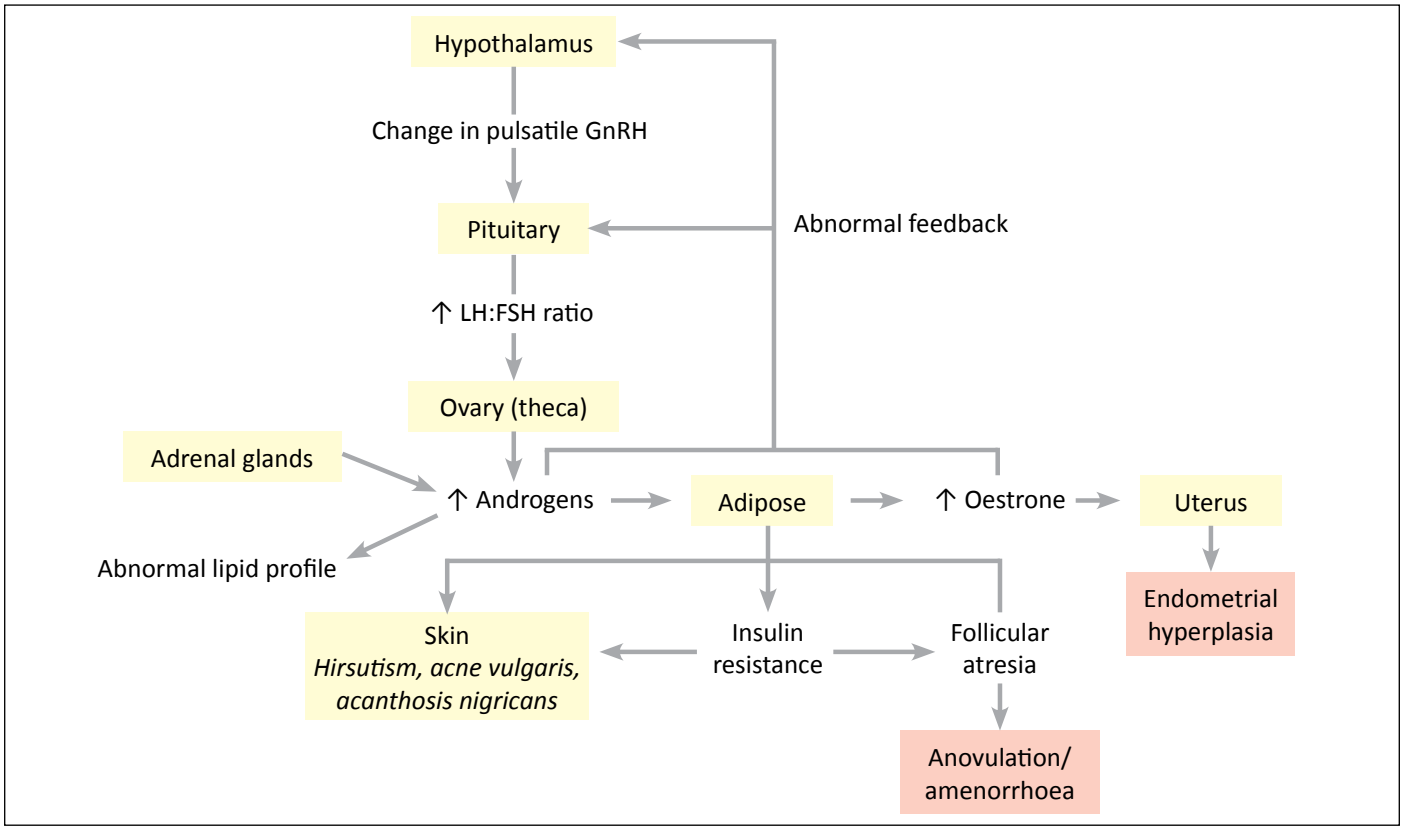


Figure 1. *The flow chart above details the suggested pathophysiology of polycystic ovary syndrome. Endocrine abnormalities are thought to occur at the level of the hypothalamus, pituitary and ovary. PCOS then manifests itself in the presence of insulin resistance due to the presence of excess adipose tissue. Insulin resistance contributes to anovulatory infertility and amenorrhoea in affected women.*

patients. There is now evidence showing that adipose tissue takes part in sex steroid metabolism and that central obesity impairs a woman's reproductive capabilities even in the absence of PCOS. [6] Obese PCOS patients are more likely to experience anovulation as compared to their thinner counterparts. [4,7]

The anovulatory effect is thought to be mediated by insulin resistance which in turn leads to hyperinsulinaemia and stimulation of excess androgen production in the ovaries. The high levels of androgens in the ovaries prevents maturation of ovarian follicles. [4,8] A combination of diet and exercise leading to weight reduction of even just 5-10% has proven effective in restoring menstrual and ovulatory cycles, thus allowing these women to achieve a pregnancy. [2,9] Furthermore, reduction in obesity improves the woman's response to other pharmacological ovulation induction methods. However, many obese women have reported difficulty in maintaining weight loss which may be a reflection of inherent metabolic disturbance in these patients. As such, PCOS patients are currently encouraged to aim for gradual weight reduction which increases the likelihood of maintaining the weight that is lost. [2]

In terms of specific dietary compositions, studies comparing high carbohydrate (55%), low protein (15%), hypocaloric diets and low carbohydrate (40%), high protein (30%), hypocaloric diets have shown similar weight loss and circulating androgen and insulin levels, thus suggesting that patients can follow either dietary composition. [10,11] Later studies have suggested that a high protein, low glycaemic index diet is effective for long-term weight reduction. [12] As a whole, the present consensus is that calorie restriction is essential but specific dietary recommendations still require more evidence. Regular exercise is also essential as it increases insulin sensitivity and resting metabolic rate, thus helping to both achieve and maintain weight loss. [6,13] Finally, other lifestyle factors such as smoking, alcohol intake and excessive caffeine consumption will also need to be addressed.

Medical therapy

Anti-oestrogen therapy

Anti-oestrogens such as clomiphene citrate (CC) are commonly used to induce ovulation. CC is thought to bind with and block oestrogen receptors in the hypothalamus, thus resulting in a perceived drop in the level of endogenous oestrogen. [14] This in turn triggers a rise in gonadotrophin secretion and subsequently, ovulation. In fact, CC has been the first-line agent for ovulation induction for over 40 years. CC has been shown to be six times more effective than a placebo at inducing ovulation and successfully does so in 50-70% of cases. [15,16] About half of these ovulations result in pregnancies and the disparity between the figures can be attributed to the anti-oestrogenic effect of CC on the endometrium and cervical mucus as well as by the resultant hypersecretion of luteinising hormone. [4,17]

Side effects of CC include a 6% chance of having a multiple pregnancy (2% background risk), vasomotor symptoms such as hot flushes and unusual visual disturbance and an increased risk of developing ovarian tumours if the patient is exposed to over twelve cycles in a lifetime. [2] There is also a small increase in the risk of developing Ovarian Hyperstimulation Syndrome (OHSS). [4] At present more evidence is needed to determine the length of treatment and effectiveness of anti-oestrogen therapy in assisted conception cycles. [18]

Gonadotrophins

Gonadotrophins (that is, follicle-stimulating hormone) are considered second-line therapy and are used when CC fails to achieve ovulation or a pregnancy. Gonadotrophins come in the form of daily injections and are particularly useful in controlled ovarian stimulation for assisted reproduction techniques. However, they are very potent and will stimulate multiple follicles simultaneously, thus increasing the risk of OHSS and multiple pregnancies. As such, ovarian response needs to be monitored using ultrasound and serum oestradiol measurements. Ultrasound monitoring alone has been shown to reduce the rate of multiple pregnancies and has a good predictive value for the development of OHSS. [18] In addition, a 'low-dose step-up' protocol has been established in fertility practice to minimise the risk of multiple pregnancies. [19]

Insulin sensitisers

Metformin is a commonly used treatment for type two diabetes mellitus. It suppresses hepatic gluconeogenesis, reduces gastrointestinal glucose absorption thereby enhancing weight loss and increases peripheral insulin sensitivity. [4] Given that insulin resistance and hyperinsulinaemia are important factors in the pathogenesis of PCOS, studies have sought to establish the role of metformin in treating infertility due to PCOS. However, studies comparing metformin with CC have been inconclusive due to the variability of their outcomes.

A randomised control trial (RCT) by Kashyap, Wells and Rosenwaks [20] concluded that metformin was beneficial for induction of ovulation and that addition of metformin to CC might increase rates of ovulation and pregnancy by three to four times. Other RCTs found the addition of metformin to CC to be of no benefit in achieving pregnancy. [21,22] Furthermore, metformin causes gastrointestinal intolerance in 40% of subjects and takes a substantially longer time to achieve a pregnancy when compared to CC. In view of this, some groups have recommended the use of metformin only as an adjunct and in women who have glucose intolerance, CC resistance or a high BMI. [18,23]

Aromatase inhibitors

Third-generation aromatase inhibitors (AI) such as anastrozole and letrozole block the conversion of testosterone and androstenedione to oestradiol and oestrone, thus augmenting pituitary feedback on gonadotrophin secretion. AIs may be used alone or in combination with CC or a gonadotrophin, in which case a lower dose of the latter is required. AIs have been found to be as successful as CC in generating follicles and achieving pregnancies and do not have the anti-oestrogenic effects observed in CC, such as endometrial thinning or cervical mucus changes. [24,25] However, some studies involving rats have raised questions about the safety of AIs in pregnancy as these studies found an increased incidence of cardiac and bone abnormalities in foetuses exposed to letrozole. [26] Therefore, until further research is conducted AIs should be used with caution and only after appropriate counselling due to the potential medico-legal implications of this medication.

Surgery

Laparoscopic ovarian drilling (LOD) is another second-line therapy. Ovarian drilling is thought to trigger resumption of menstrual cycles and ovulation by reducing ovarian theca cells and, by extension, serum androgens and luteinising hormone. [4] Since ovarian drilling has a similar efficacy to gonadotrophin therapy but has significantly less risk of inducing OHSS, the UK National Institute for Health and Clinical Excellence has advised that women resistant to CC should undergo ovarian drilling in order to avoid the risk of multiple pregnancy. [27,28] A recent RCT of five-, ten- or fifteen-puncture ovarian drilling concluded in favour of the fifteen-point puncture to each ovary in order to resume ovulation and pregnancy. However, current data only includes pregnancy rates and there is no data on live birth rates. Furthermore, as with any surgical procedure, there is a risk of complications such as adhesions, anaesthesia risks and other operative morbidities. The long-term effect of such aggressive ovarian insult has also not been established. [29]

In-vitro fertilisation

IVF tends to be reserved for women with PCOS who have failed to become pregnant following gonadotrophin therapy. [2] Women with PCOS who undergo IVF are seven times more likely to develop OHSS. One way of avoiding this is by inducing maturation in vitro after oocytes are collected from the unstimulated ovaries of a woman during a cycle. [30] Women with PCOS respond very well to ovarian stimulation and therefore tend to perform well in IVF cycles. [4]

Management of patients with clomiphene citrate-resistance

The current expert-based recommendation for first-line treatment of infertility due to PCOS is ovulation induction with CC for up to six ovulatory cycles, with the addition of metformin where there is glucose intolerance. [23] CC administration begins on day two or three and comprises a 50mg/day dose with increases of up to 150mg/day with each unsuccessful cycle. If ovulation still has not occurred at the maximum dose, the patient is considered 'clomiphene citrate-resistant' and alternative treatments will be introduced. Table 1 outlines the various traditional and alternative treatment regimes including dosing regimens where a general consensus has been found.

Metformin is the most commonly used adjunct to CC. Other adjuncts such as dexamethasone have been shown to have some benefits but are not commonly used in clinical practice and therefore have not been included in Table 1. [16,31] At present, AIs appear to be one of the more promising treatment alternatives to CC due to their efficacy in achieving ovulation and pregnancy as well as their lack of anti-oestrogenic side effects. However, more research is needed investigating the optimal dose required and the effect of AIs on the foetus.

Conclusion

In conclusion, the prognosis for women with PCOS-related infertility remains excellent due to the various treatment modalities that are currently available. However, there is still a significant level of inconsistency when the effectiveness of each therapeutic modality is evaluated. This inconsistency is partly due to the differences in definition of primary and secondary outcomes as well as the variety of settings in which various therapies are investigated. Furthermore, while most studies have used ovulation and pregnancy rates as the measurable outcome, only a few have actually included the most relevant primary outcome, live birth rates. Finally, more research is needed to determine the dosage regimes and long-term health consequences of the various treatment modalities. Clinicians should also take into account the costs and side effect profile when choosing a suitable treatment for women with infertility due to PCOS.

Conflict of interest

None declared.

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Table 1. *Outline of traditional and non-traditional therapeutic options for women with PCOS-related infertility, with dosing regimens included where there is general consensus on the treatment.*

Therapy	Dosing Regimen	Advantages/Disadvantages
Traditional Therapy		
First-line therapy Clomiphene citrate	Five days starting at day two or three of cycle. 50mg/day at first cycle, dose can be increased to 150mg/day over six cycles.	Very effective. High level of clinician familiarity. Has anti-oestrogenic effects which affect pregnancy rates.
Second-line therapy Gonadotrophin	Daily injection.	High risk of multiple pregnancies and OHSS. High level of monitoring required. Expensive.
Second-line therapy Laparoscopic ovarian drilling (LOD)	Four- to fifteen-puncture LOD followed by three months observation. In patients who are still anovulatory, three further cycles of CC may be considered.	General risks associated with surgical procedures. Cheaper than gonadotrophins. Increases ovarian response to gonadotrophins. Reduced risk of OHSS.
Alternative therapies		
Insulin-sensitising drugs Metformin	Metformin only	Metformin is approximately twenty times cheaper than LOD.
	Metformin or other insulin-sensitisers plus CC	Metformin plus CC may be even more effective than LOD in achieving ovulation and pregnancy.
	Metformin plus gonadotrophin	Some evidence of more orderly follicular growth, reduction in multifollicular development, reduced risk of OHSS.
	Metformin plus letrozole	Similar rates of ovulation, number of mature follicles and pregnancies to metformin plus CC. Significantly higher endometrial thickness and full-term pregnancies than metformin plus CC.
Aromatase inhibitors Letrozole	Five days starting from day three of cycle, 2.5mg/day letrozole. OR Single dose 20mg on day three of cycle.	Ovulation induction without anti-oestrogenic effects. May be embryotoxic. More evidence needed.
Clomiphene citrate combinations	Pre-treatments: Metformin	Thought to sensitise patients to CC. Two months of hypothalamic-pituitary-ovarian axis suppression followed by administration of CC has been shown to be even more effective at inducing ovulation and achieving pregnancy than CC alone.
	Combinations: CC + metformin	Improves insulin sensitivity and decreased hyperandrogenaemia.

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Prevention of rheumatic heart disease: Potential for change

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Jovita is a fourth year medical student (2011) from James Cook University with a great interest in research, mainly in the field of paediatric cardiology. She aspires to undertake an Honours project in the field of cardiology. After moving to the tropics and seeing cases of Rheumatic Heart Disease, Jovita became highly passionate in looking at its prevention. She believes that Rheumatic Heart Disease is still an important issue that should not be forgotten.

Rheumatic heart disease (RHD), an autoimmune reaction to an infection of rheumatogenic group A streptococcus bacteria, is characterised primarily by progressive and permanent heart valvular lesions, although other parts of the heart may be affected. Despite an overall decrease in the incidence of RHD in developed countries, it remains a pertinent health issue with high rates in developing countries and amongst certain Indigenous populations in industrialised countries. Primary, secondary and tertiary strategies for the prevention of rheumatic heart disease exist, as do numerous barriers to such strategies. A review of the literature, incorporating its epidemiology and pathophysiology, demonstrates that interventions at various stages of the disease may reduce the collective burden of disease.

Introduction

Rheumatic heart disease (RHD) is a chronic condition characterised by fibrosis and scarring of the cardiac valves and damage to heart muscle. It arises from an episode or recurrences of acute rheumatic fever (ARF), an immune-mediated multisystem inflammatory disease. ARF is caused by infection with rheumatogenic group A streptococcus bacteria. [1,2] One of the most serious manifestations of ARF is carditis, which is evident in approximately 30-45% of people with rheumatic fever. [3,4] Although the severity of rheumatic carditis varies widely between individuals, it is usually the main contributor to the morbidity and mortality of rheumatic fever. This is due to the permanent and progressive nature of damage it causes to the heart, ultimately leading to rheumatic heart disease. [3,5]

The diagnosis of rheumatic heart disease is most effectively determined through the use of echocardiography. The patient may present with various signs including pericardial rub, tachycardia, an apical systolic murmur consistent with mitral regurgitation, a basal diastolic murmur consistent with aortic regurgitation or severe congestive heart failure. [4,6] The most commonly affected valve is the mitral valve, affected in 65-70% of patients, followed by the aortic valve, affected in 25% of patients. Damage to the tricuspid valve is typically associated with mitral and aortic valvular lesions. Severe dysfunction of the cardiac valves can lead to congestive heart failure and death. [7,8]

The incidence of rheumatic heart disease is estimated at 15.6 to 19.6 million cases worldwide and it is responsible for over 233,000 deaths annually. [3,9,10] RHD is a major public health problem particularly in developing countries, which account for over 80% of cases of ARF and RHD. [11] Whilst the incidence of ARF and RHD has decreased in most developed countries, cases are disproportionately high amongst the Indigenous populations in these countries. [3,11] It may thus be concluded that this disease affects populations universally and is a pertinent issue to address and prevent. This review will explore different preventative strategies and barriers to these preventative measures.

Pathophysiology

Rheumatic heart disease is characterised by heart valve damage and is the consequence of rheumatic fever, an acute immune-mediated inflammatory disease triggered by untreated Group A streptococcal (GAS) pharyngitis. [12] Rheumatic fever causes permanent damage

to cardiac valves, particularly the mitral and aortic valves, leading to rheumatic heart disease. Pathological findings include thickening of the valve leaflets and chordae, mitral annular dilation and chordal dilation. [3,13] Multiple episodes of rheumatic fever cause additional damage to cardiac valves and exacerbate rheumatic heart disease. [14] It has been estimated that 60% of those with ARF will develop RHD. [11,15]

GAS is a gram-positive bacterium that attaches to the epithelial cells of the upper respiratory tract, eliciting an acute inflammatory response within three to five days. Patients typically present with a sore throat. [16] In 0.3-3% of cases, rheumatic fever occurs as a consequence of the infection and it is generally believed that only infections of the pharynx can cause rheumatic fever. [17,18] However, emerging studies have suggested that GAS impetigo could also lead to rheumatic fever. McDonald *et al.* [19] found that in some Indigenous Australian populations with a high incidence of ARF, there is a low incidence of GAS pharyngitis but a high incidence of GAS impetigo. In other high-incidence ARF populations, an absence of rheumatogenic M-serotypes of GAS may suggest that other serotyopes, including those causing GAS impetigo, may be involved. [11] Although it is widely accepted that only certain strains of GAS leads to rheumatic fever, the mechanism of how the initial infection develops into rheumatic fever remains unclear. [7,9]

Rheumatic fever is mediated by molecular mimicry between beta haemolytic streptococci and host tissue epitopes. [19] There are many GAS antigens that are believed to be cross-reactive epitopes including the M protein and N-acetyl glucosamine. These antigens share epitopes with human cardiac tissue, including the alpha-helical cardiac proteins including myosin, laminin and vimentin. [3,11,20] Recent studies conducted on rats support the similarity between components of M proteins found in certain strains of GAS and human tissue epitopes. [9] The anti-streptococcal antibodies that are produced by B cell lymphocytes cross-react with the host tissue epitopes by binding to the endothelial surface, leading to inflammation, cellular infiltration and valve scarring. Peptide fragments from the bacteria are also presented to T cell lymphocytes via major histocompatability complex (MHC) molecules, generating an immune response. [3,20] Guilherme

et al. [20] found that 91% of heart tissue biopsies revealed cellular infiltration consisting predominantly of CD4+ T cells. In addition, upregulation of vascular cell adhesion molecule-1 (VCAM-1) and neovascularisation promote T cell migration and infiltration, thereby causing further damage to cardiac valves. [11,20]

Genetic predisposition has been suggested to play a role in the autoimmune response against GAS, with an estimated 3-15% of any population being genetically susceptible to ARF. [9] Autoimmune diseases have been associated with several human leukocyte antigen (HLA) class II alleles which are expressed on antigen presenting cells. The antigen presenting cells are in turn responsible for presenting pathogenic antigens to, and consequently activating, T and B lymphocytes. The allele most commonly found to be associated with ARF and RHD is HLA-DR7, which may associated with to the occurrence of multiple valvular lesions. [3,20] Additionally, the tumour necrosis factor-alpha (TNF-α) gene, which is located close to the HLA class II genes, is related to inflammatory responses. The presence of this allele suggests a link to the development of rheumatic heart disease. [20]

Epidemiology

Rheumatic heart disease causes an estimated 233,000 deaths per year with approximately 282,000 newly diagnosed cases annually. The first episode of ARF typically occurs in those aged five to fourteen years old. Of the 15.6 to 19.6 million cases of RHD worldwide, 2.4 million cases occur in this age group. [3,8] In many developing countries, RHD is the most common cause of acquired heart disease in children and young adults. However, it still affects developed countries, particularly the Indigenous populations of these countries. [11,21]

Developing Countries

ARF and RHD affect an estimated 20 million people in the developing areas of the world and are the leading causes of cardiovascular death in the first five decades of life. [12] Ninety-five percent of new cases and deaths due to RHD each year occur in the developing world. [10] Epidemiological data from developing countries is poorly documented. It may therefore be the case that case numbers are higher than those recorded in the data. Many studies conducted in these countries have used data from school-aged children. [8]

The estimated annual number of cases of ARF amongst children aged 5 to 14 years old is 374 per 100,000 population, with approximately 60% of these children going on to develop RHD. The highest prevalence of RHD among school children is in sub-Saharan Africa where it has been documented as 5.7 cases per 1,000 population. [8,17,21] Kyrgyzstan, located in Central Asia, has the highest prevalence of ARF and RHD of all the developing countries. Over the last ten years, mortality from ARF and RHD in Kyrgyzstan has increased by 150% among children, by 33% among adolescents and 27.5% among adults. [8] These high rates are due to factors such as low standards of living, the high number of GAS carriers and an increase in the population migrating to other areas. [21]

A study from Brazil revealed that the incidence of ARF in Brazil declined by 75% between 1992 and 2002. Despite an overall decrease in incidence, figures remain high with 5,000 new cases in 2002. [4,21] In some regions of Brazil ARF is regarded as endemic, and RHD is accountable for nearly 90% of early childhood valvular surgeries in the country. [20]

The global burden of RF and RHD amongst developing countries over the past century can be explained by the socioeconomic conditions, lack of hygiene, access to medical care and overcrowding. [22] As mentioned earlier, the possibility that GAS impetigo could also be responsible for ARF may explain the disparity between ARF in different communities; however there is no definitive evidence to support this. [17,22]

Developed Countries

Over the past 80 years, the incidence of ARF and RHD has decreased in the United States and other developed countries. [7] A systematic review of ten population-based studies, which investigated the worldwide incidence of ARF between 1967 and 1996, found the lowest incidence rates in American and Western European nations. [3] The prevalence of RHD in the United States is now less than 0.05 per 1,000 population. [7] The overall decline in these areas of the world is due to improvements in aspects of primary prevention such as access to healthcare, housing conditions and appropriate use of antibiotics. It has also been suggested that the decreased incidence of ARF in the United States over the past 50 years is related to the replacement of rheumatogenic strains by non-rheumatogenic strains in cases of streptococcal pharyngitis in children. However, the reason for the change in distribution remains unclear. [12,19]

Indigenous Populations

ARF and RHD are not endemic in developing countries alone. They also affect industrialised countries, particularly within certain population groups. Various studies have demonstrated that in developed countries, the rates of ARF and RHD are vastly higher in Indigenous populations including Aboriginal Australians, Maoris of New Zealand, Native Americans and Hawaiians in the United States. [5]

The highest documented rates of ARF and RHD in the world occur in Indigenous Australians living in the "Top End" of the Northern Territory. [14] Aboriginal and Torres Strait Islanders are 8 times more likely than non-Indigenous Australians to be hospitalised for ARF and RHD and nearly 20 times more likely to die from causes related to the disease. [23,24] The increased susceptibility is due to the socio-economic and health statuses of Indigenous Australians, which are generally lower than those of the non-Indigenous population. One study reported that in two different communities in the Northern Territory the median number of people per household was 14 to 17 and concluded that this was a contributing factor to the high rates of ARF and RHD. [22]

Prevention

Primary Prevention

The purpose of primary prevention is to avoid the initial development of RHD. RHD is a consequence of ARF and hence primary prevention should be focused upon preventing ARF through timely diagnosis and treatment of GAS infections. Over 50 years ago, during epidemics approximately 3% of untreated streptococcal sore throats resulted in rheumatic fever. The dramatic reduction in ARF and RHD in developed countries since then is thought to be the result of improvements in socioeconomic conditions such as hygiene, access to medical care and reduced overcrowding. [11,23] Another factor which has led to the decline of ARF in developed countries is the widespread availability and use of antibiotics to treat GAS infections, which greatly reduces the chance of developing ARF. [5] Poor socio-economic conditions in developing countries and amongst certain populations within developed areas result in an increased susceptibility to ARF. However, it is important to acknowledge that ARF is not a disease that only affects these populations, as there are microbiological, immunological and genetic factors involved. [3] A successful vaccine against rheumatic heart disease is yet to be developed but is a future prospect.

While improving the socioeconomic status of high-risk populations is beneficial in reducing the circulation of GAS, the main focus has been placed on treating GAS infections appropriately. An accurate diagnosis of GAS pharyngitis is vital and usually involves microbiological confirmation via a throat culture or a rapid antigen detection test (RADT). [12] A recent systematic review found that the risk of ARF was reduced by 70% if antibiotics were given to patients with sore throats and symptoms indicative of a streptococcal infection. The risk was further reduced by 10% if intramuscular penicillin was given. [17] The recommended guideline for managing an initial attack of ARF is a single intramuscular dose of benzathine benzylpenicillin as a prophylactic agent against recurrent episodes and for the eradication of Group A streptococcus if it is still present. [9]

A correct diagnosis of ARF is also imperative to prevent RHD from occurring. The diagnosis is based on clinical criteria, known as the Jones Criteria, shown in Table 1. These criteria have been suggested to result in the under-diagnosis of ARF in high-incidence populations due to their strict application, as reported by epidemiologists and clinicians working in developing countries and Indigenous populations in developed countries. A modified set of criteria targeted at high-risk groups has been proposed to increase sensitivity. [11]

Table 1. *Modified Jones Criteria for the diagnosis of ARF. [25] For the diagnosis of ARF: 2 major or 1 major and 2 minor manifestations plus evidence of a preceding GAS infection are required.*

Major manifestations	Minor Manifestations
Carditis	Fever
Migratory polyarthritis	Arthralgia
Sydenham's Chorea	Elevated acute phase reactants
Erythema marginatum	Prolonged P-R interval on ECG
Subcutaneous nodules	

Secondary Prevention

Secondary prevention of RHD involves preventing recurrent attacks of ARF and treating the disease in its initial stages to avoid further damage. Rajamanan *et al.* [8] suggest that medical therapies for patients in the early stages of RHD may slow the progression of RHD affecting the valves.

An individual with a history of rheumatic fever who develops GAS pharyngitis is at high risk of suffering from a recurrent attack of ARF. Recurrences of ARF can exacerbate the severity of RHD from previous attacks or, less commonly, may result in the new onset of RHD in individuals who have not experienced cardiac manifestations. A study conducted by Meira in Brazil observed a group of children and adolescents by clinical examination and echocardiography for 5.4 years after their initial episode of ARF. They found that one of the risks of developing chronic RHD was a history of recurrent episodes of ARF. Preventing recurrent attacks of ARF has been shown to be the most successful and cost-effective way of preventing RHD. [3,25]

The recommendation for preventing recurrent attacks ARF is a continuous dosing regime of intramuscular benzathine benzylpenicillin every four weeks, and every three weeks in high-risk populations. This strategy has been shown to lead to regression of existing heart valve lesions and reduce RHD mortality. [25] Studies in Taiwan have shown that three-weekly instead of four-weekly injections reduced the number occurrences of ARF; however compliance with such frequent dosing is poor. American, Australian and New Zealand guidelines recommend four-weekly injectable benzathine penicillin G with three-weekly injections for patients who have a recurrent episode despite adherence with the four-weekly regime. [11] It is suggested that prophylaxis should be continued for at least five years after the initial attack as the chance of recurrence is the highest during this time period. However, more recent guidelines suggest a continuing with the regimen for a minimum of 10 years or until the age of 21, depending on which time length is longer. [3,11] Although the risk of RHD increases with multiple previous attacks of ARF, it decreases as the interval since the most recent attack lengthens. [12]

For early treatment of RHD, an accurate diagnosis must be made promptly. The diagnosis of RHD was previously made on the basis of clinical history and physical findings. However, echocardiography has since been introduced as the diagnostic standard following several reports showing that clinical examination alone lacks sensitivity in detecting RHD in high-risk populations. [26] Shiffman [27] revealed that despite 50 years of technological and methodological advances in medicine, echocardiography along with new antibody testing are the only new components of knowledge that have influenced the diagnosis of ARF. Studies conducted on children in Cambodia and Mozambique by Marijon *et al.* found that echocardiography detected ten times the number of cases of RHD compared with clinical examination alone. [5,27,28] Carapetis *et al.* [29] found that auscultation missed 54% of those with RHD and an accurate diagnosis of RHD was significantly higher if echocardiography was used after an abnormal murmur was detected through clinical examination. [3,29]

Tertiary Prevention

Tertiary prevention of RHD is achieved through monitoring and managing the disease. Once the heart valves have been damaged, tertiary prevention may prevent further damage from occurring. This can be accomplished by patients having regular health check ups and undergoing surgery if appropriate.

Surgery is recommended in adults who have symptoms of severe mitral incompetence or if they have reduced left ventricular function or a left ventricular end systolic diameter of 40mm or greater. There are various interventions for mitral stenosis including closed mitral valvotomy, open mitral valvotomy and interventional mitral valvotomy, although such procedures are not curative. [2] Valve repair has been demonstrated to be more effective than valve replacement due to the risk of complications of prosthetic valves, including thromboemboli, bleeding, teratogenic events associated with warfarin administration and the poor durability of bioprosthetic valves in younger patients. [17]

Barriers

Barriers exist to the effective prevention of rheumatic heart disease. Firstly, at least one third of episodes of ARF result from asymptomatic streptococcal infections, making it difficult to detect and appropriately treat the disease. [12] This may be partly attributable to a lack of access to medical care. Further, as previously suggested, an accurate diagnosis is necessary to treat GAS pharyngitis. This may be challenging in developing countries due to limited resources.

If diagnosed correctly, there are challenges to ensuring correct treatment and compliance. [11] Whilst primary prevention programs aim to educate at-risk populations about the importance of early presentation and treatment compliance along with health professional awareness, there are problems with sustaining such programs over a long period of time. [5] Barriers to secondary and tertiary prevention of RHD include the availability of medication, monitoring tests, cardiothoracic surgery and intervention facilities. [11] As the disease progresses to a chronic stage, continued medical and surgical treatment becomes costly for the patient, their family and society. [10] In addition, as emerging studies have suggested that GAS impetigo may also play a role in the pathogenesis of ARF, changes to primary prevention strategies which currently focus on GAS pharyngitis would need to be made.

Future possibilities for prevention

Clinical trials for an effective GAS vaccine have been conducted, as this would prevent GAS infection and thus the development of ARF and RHD. [9] Although multivalent M type specific vaccines have shown evidence of safety and immunogenicity, they may have limited efficacy due to the existence of numerous rheumatogenic M protein serotypes. [11,17]

Conclusion

It is evident that RHD poses as a pertinent issue across certain populations in developing and developed countries, including Australia. Hence, it is a disease that is of relevance on a global level. This review investigates the primary, secondary and tertiary prevention strategies that are most beneficial for RHD. It also outlines the pathophysiology of RHD to aid with the understanding of how the disease occurs and progresses as well as to emphasise the magnitude of the problem by examining its epidemiology. Treatment of RHD has not changed significantly over the past fifty years; however, the current treatment of streptococcal infections should remain while other strategies are being trialed. It is essential for research to continue in this area,

particularly for the development of a cost-effective vaccine, in order to greatly reduce the burden of RHD globally.

Conflict of interest

None declared.

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Human papillomavirus in head and neck squamous cell carcinoma

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Ross is keenly interested in surgical oncology, particularly in relation to ear nose and throat surgery. He also has research interests in venous ulceration. He is to spend the remainder of his medical degree at the Townsville Clinical School.

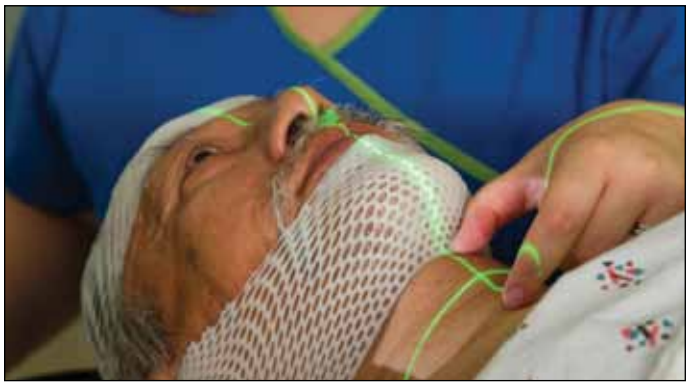
Background: Head and neck squamous cell carcinoma (HNSCC) is a significant global health burden. Approximately 25 percent of HNSCC cases are caused by human papillomavirus (HPV). These particular cancers of viral aetiology have been found to have distinct characteristics in regards to presentation, treatment and prognosis. Current advances in vaccinology have the capability to drastically decrease the incidence of HPV-positive HNSCC. **Methods:** A literature review was undertaken through MEDLINE/PubMED/Ovid databases. The terms "HPV," "HNSCC," "carcinogenesis," "treatment," "prognosis" and "vaccine" were searched. Only studies published in English were considered with 65 articles selected and analysed. Preference was given to studies published in the last ten years. **Results:** The incidence of HPV-positive HNSCC is increasing. Infection with HPV can result in cancer through the expression of oncogenic proteins which disrupt normal cellular turnover. Aggressive treatment is often undertaken causing significant morbidity in many patients. A proportion of patients die from this disease, suggesting that these cancers have a considerable impact on society. **Conclusion:** Human papillomavirus is an infectious agent that is likely transmitted through skin-to-skin contact. The virus integrates into the DNA of the host with the high oncogenic risk genotypes, HPV 16 and 18 being strongly linked to HPV-positive HNSCC development. Prevention through vaccination against these genotypes is currently an option for all individuals. The cervical cancer vaccines immunise non-exposed females against HPV 16 and 18. Vaccination of both males and females will prevent HPV-positive HNSCC.

Introduction

Cancers of the head and neck are diagnosed annually in more than half a million people worldwide. These cancers represent the fifth leading cause of cancer by incidence and sixth leading cause of cancer mortality. [1,2] More than 90 percent of head and neck cancers (HNC), which are defined as those cancers arising from the upper aerodigestive tract, are pathologically identified as squamous cell carcinoma (SCC). [3,4] Whilst the carcinogenesis of head and neck squamous cell carcinoma (HNSCC) has primarily been attributed to environmental factors such as tobacco and alcohol, evidence has implicated a subset of these cancers are directly resultant from infection with human papillomavirus (HPV). [5-7]

Considerable research has been conducted in recent years to understand HPV-positive HNSCC as well as other HPV-associated cancers. Studies have suggested that HPV is a sexually acquired infection, with the virus resulting in an oncogenic mechanism which causes cancer in some individuals. [8] Epidemiological data of HPV-positive HNSCC has revealed a recent increase in the incidence of these cancers as well as a reduction in the median age of presentation. [8-11] Additionally, the treatment of these cancers is challenging and often results in disfigurement, physical disability and psychosocial morbidity in patients whom are fortunate enough to survive. [1,12]

The opportunity to decrease the incidence of HPV-associated cancers such as HNSCC has been highlighted by political and public attention generated since the introduction of HPV vaccination programs throughout the world to prevent cervical cancer. [13,14] As these programs target young women, the purpose of this review is to discuss



the role of HPV in HNSCC so as to educate healthcare workers on the importance of the announcement in Australia that young males will also be vaccinated against HPV.

Body

Background

Human papillomaviruses were first described as having a carcinogenic effect in a seminal study by Orth *et al.* in 1979. [15] However, it was not until 1983 that Syrjänen and colleagues suggested HPV as having a specific role in the pathogenesis of HNC. [16] From this research, studies have investigated the link between HPV infection and subsequent HNC, with SCC of the oral cavity, [6] pharynx, [9] and larynx [17] all being described. These findings, as well as other research implicating HPV in cancer of the penis, [18] cervix, vagina, vulva and anus have allowed significant insight into understanding HPV. [19,20]

Human Papillomavirus Virology

The virology of HPVs has uncovered that they are small, non-enveloped, double-stranded DNA viruses belonging to the Papillomaviridae family, with more than 120 different genotypes being described. [21] Research has categorised these HPVs into those which have a high carcinogenic risk associated with invasive cancer, whilst another group has been termed low risk or non-oncogenic. [4,22,23] Infections with the high risk genotypes, HPV 16 and 18, have become an increasing focus in head and neck carcinogenesis research.

Human Papillomavirus genotypes in head and neck squamous cell carcinoma

Studies investigating the exact role HPV infection plays in the development of HNSCC have consistently found that, overall, approximately 25 percent of HNSCC cases are associated with infection. [3,4,24] Furthermore, the degree of participation each individual genotype has in developing HNSCC has recently been reported in a large meta-analysis encompassing more than 5,000 cases. The high risk genotypes HPV 16 and 18 were found to be strongly implicated in HPV-positive HNSCC, with the authors uncovering that HPV 16 was responsible for the majority of cases. [4] This finding has been repeatedly demonstrated within the literature with studies reporting that HPV 16 is involved in 85 to 95 percent of HPV-positive specimens. The remaining cases comprising HPV-positive HNSCC have been found almost exclusively to be caused by infection with HPV 18. [1,22,24]

Infection

Understanding the exact route of transmission of these high risk HPVs

to the upper aerodigestive tract has lead to the knowledge that HPV is a sexually acquired infection. [8] One study conducted found that of 15.4 million cases of sexually transmitted infections, 5.5 million of these cases were from HPV. [25] Behaviours such as increasing numbers of lifetime vaginal or oral sex partners, a history of other sexually transmitted diseases, a history of casual sex, early age of sexual debut and the lack of using barriers during vaginal or oral sex have all being associated with HPV infection and HPV-positive HNSCC. [7,26] Research has suggested that HPV is only able to survive in certain epithelial sites, including lymphoid tissue, and this tissue may represent a reservoir for HPV infection. In regards to the upper aerodigestive tract, tonsillar tissue has been proposed to harbour HPV which has the possibility of inoculating sexual partners. [27]

Carcinogenesis

Whilst the vast majority of infections with the high risk HPVs are eliminated by the immune system and are therefore asymptomatic, studies have revealed that in some cases persistent infection can lead to cancer development. [28] The current carcinogenesis model that has been proposed suggests that HPV results in the initiation of cancer development, with a multitude of steps being involved in the progression to HPV-positive HNSCC. [29]

The commencing step in HPV-positive HNSCC development is viral infection of basal epithelial cells through wounds or abrasions by invading the actively dividing cells in the area. [22] In the vast majority of cases the HPV DNA is then integrated into the host cell genome which causes two viral genes to be expressed. The two viral genes are known as E6 and E7 with research implicating their expression with mutations from a proliferative perspective. [29]

It has been found that the expression of E6 and E7 in humans is sufficient and necessary for immortal transformation of keratinocytes. [30] The E6 protein is known to bind to, and induce, the degradation of the p53 tumour suppressor protein. [22,31] This protein plays a critical role in controlling cell growth by regulating cell cycle progression and responds to stress via apoptosis. [31] Meanwhile, the E7 protein has been found to have a role in disrupting the retinoblastoma (Rb) pathway. [22] The HPV E7 oncoprotein binds to and causes destabilisation of the Rb protein and the transcription factor E2F complex. This results in the release of E2F which is then able to act on cellular proliferation genes and thus increase the level of cellular division. [32]

Furthermore, research has also discussed the fact that genetic influences play a role in the development of HPV-positive HNSCC. One recent study by Chen *et al.* described that genetically susceptible individuals may be at increased risk of HPV 16-positive HNSCC. [33] The article suggests that alteration in vitamin C metabolism, manifested by the altered transporter SLC23A2, modifies the likelihood of HPV 16 infection and subsequent HNSCC development. [33]

In addition to host genetic susceptibility there is also a relationship between extrinsic factors and HPV infection. Although this issue remains somewhat controversial, [6] research has reported that HPV-positive individuals whom are smokers have a greater risk of developing HPV 16-positive HNSCC. [34,35] The complexity of the carcinogenesis is also complicated by the impact of alcohol consumption. In those people who drink, there is an increased tendency for collagenase activity thus leading to increased likelihood of invasive cancer. [36,37] It is therefore apparent that although the cellular proliferation of HPV-positive HNSCC has been well described, other influences may be involved in the carcinogenesis of HPV-positive HNSCC and this suggests that the disease may be multi-factorial. [38]

Presentation

The sites of presentation of HPV-positive HNSCC development are varied, with all areas of the upper aerodigestive tract being observed in the clinical context. [1] Due to the large variation of cancer sites affected, a range of clinical presentations are evident in patients. One principal aspect of HNC that requires particular consideration by primary care physicians is that of the presence of a painless enlarging neck mass. [39,40] This requires attention and work-up by specialist practitioners involving physical examination and diagnostic imaging which generally includes a combination of computerised tomography (CT), magnetic resonance imaging (MRI) and fluorodeoxyglucose positron emission tomography (PET) focusing on the area of interest. [40-43] Additionally, a panendoscopy under general anaesthesia is often performed with biopsy samples taken. [44]

Regardless of the site of origin that HPV-positive HNSCC develops, a number of common trends have been uncovered using the tumour-node-metastasis (TMN) staging system for HNC. In one study by Paz *et al.*, 83 percent of HPV-positive HNSCC were reported as having positive lymph nodes, whilst only 44 percent of HPV-negative HNSCC had positive lymph nodes.[41,44] Furthermore, it has also been uncovered that patients diagnosed with HPV-positive HNSCC often present with tumours of a larger size. [1] Considering these facts, it is clear that HPV-positive HNSCC presents at higher stages of disease.

Treatment

The overall complex vital anatomy and functional processes that occur in the head and neck area, as well as advanced stages of presentation of HPV-positive HNSCC make the management and treatment of these cancers difficult. [45] Numerous medical specialities and allied health professionals, including clinical psychologists provide input into the care of people diagnosed with HPV-positive HNSCC. The primary goal of all healthcare professionals involved is to improve the survival of the patient, as well as preserving organ function. [45]

Following the initial cancer diagnosis, patients are staged according to the TMN system. In individuals that present in early stages, which include stages 1 and 2, the treatment aim is curative and employs radiation therapy or surgery as a single modality. However, in those patients that present in stages 3 or 4, the management is challenging and based on assessing functional outcomes and competing morbidities. [1,46]

Treatment of advanced HNC, which has been noted to be more prevalent in HPV-positive HNSCC, previously employed surgical resection followed by radiation therapy. [46] However, this approach has been altered in recent times with one of two approaches being employed. The first option involves undertaking surgery and the patient receiving post-operative chemoradiation; whilst the second option is that of the patient receiving chemoradiation initially with surgical salvage being performed only if required. [46,47]

There has also been the more recent suggestion within the literature that transoral robotic surgery particularly in the management of oropharyngeal SCC may offer improved clinical outcomes. In one study by Moore *et al.*, [48] 45 patients with oropharyngeal SCC underwent transoral robotic surgery, with the study describing no major complications or no need to abort the surgery. Suggestions have been made that this surgery is a safer and more efficacious method of surgical treatment with very low estimated blood loss, decreased length of hospital stay and the enhanced ability of patients to retain or rapidly regain oropharyngeal function. [48,49] These results are suggestive of a shift in the management of oropharyngeal SCC and have implications for those patients diagnosed with HPV-positive HNSCC. [50]

In addition to these therapies, treatment targeting epidermal growth factor receptors (EGFR) has emerged in protocols of locally advanced HNSCC. [1] A monoclonal antibody against the EGFR called cetuximab has been developed and has proven effective in improving locoregional control and overall survival in combination with radiation therapy. [51] It should also be noted that in those patients that present with metastatic disease and are too advanced for curative action to be undertaken, palliation of symptoms and prolongation of life is generally achieved by using chemotherapeutic agents. [39,46]

Prognosis

The numerous treatment options that are currently available have all been associated with significant psychological and physical morbidities. Problems such as mucositis, xerostomia, dysphagia, voice alterations and trismus have all been linked to the various modalities involved in treatment. [46,52,53] Additionally, the risk of recurrence as well as cosmetic effects related to aggressive treatments can have negative mental implications and lead to decreased quality of life. [1,53]

Despite the negative effects of treatment, research has shown HPV-positive HNSCC as having an improved survival when matched with HPV-negative HNSCC. [54,55] This has been primarily attributed to an increased sensitivity of HPV-positive carcinomas to all treatment options, especially radiation therapy. [45,47] In one recent study by Charfi *et al.*, [56] it was found that HPV-positive tonsillar SCC had a five year survival rate of 71 percent, compared to HPV-negative tonsillar SCC which had a five year survival rate of 36 percent. Nonetheless, it is important to keep this in perspective with many patients fortunate enough to survive this cancer often having to deal with life-long side effects from aggressive treatment. [53]

Prevention

The overall seriousness of HPV-positive HNSCC has resulted in methods of reducing the burden of these cancers to be explored. There exists a distinct need to educate the population regarding the risk of exposure to HPV associated with sexual activities. Further, the public needs to acknowledge the importance of barrier contraception for penetrative intercourse as a possible means of avoiding HPV infection, in light of research remaining unconvincing regarding the route of infection. Moreover, the utilisation of prophylactic vaccines against HPV as a primary prevention health strategy in women to prevent a proportion of cervical cancers offers a way in which to prevent HPV infection in males. [14]

Specific immune responses can be generated against HPV 16 and 18 with reports of the efficacy of these vaccines being described as between 90 and 100 percent. [13,14] The vaccine induces immunity against HPV 16 and 18 with high levels of titres of antibodies being reported 6.4 years post-vaccination. [57] Females are currently receiving these vaccines through subsidised programs, and a subsidised program has recently been announced in Australia for males. [13,58] It is expected HPV-positive HNSCC incidence will dramatically decrease in future years with the vaccination programs.

Integrated Discussion

Current literature reports that HPV is a highly infectious agent. Whilst there does not appear to be a body of evidence that refutes this finding, the exact route of transmission has yet to be confirmed. Orogenital sex has emerged as one recent theory regarding infection, [59-61] however, this view has been questioned with the finding that open-mouth kissing may explain transmission. [26] From this, it appears that this variation in studies may be explained by the fact that sexual behaviours are difficult to study. Future research should accept that skin-to-skin contact of intimate nature is the route of transmission and instead focus on developing sex education programs. This is particularly important considering the increased acceptance of discussion regarding sexual practices.

With an expected increase in the incidence of HPV-positive HNSCC into the foreseeable future, it is critical that practitioners are educated regarding the presentation of HPV-positive HNSCC. Whilst various clinical presentations have been described, it is also important to acknowledge that a younger population will likely present as people experimental with sex earlier in life, thus leading to increased possibility of HNSCC development, [1,22] as well as other HPV-associated cancers. [18,19] The current viewpoint of research has highlighted the need to fully investigate a painless enlarging neck mass and has accepted that the presentation of HNC is clinically challenging. There has been a calling for the development of non-invasive screening tools. [62] This is one area of research that is actively being undertaken and may prove advantageous in future years.

Additionally, it is well established that HPV-positive HNSCC responds more favourably to the current treatment options when compared to HPV-negative HNSCC. [55] Subsequently, there has been an appeal from the medical and scientific communities to decrease the aggressive nature of treatment for HPV-positive HNSCC in order to avoid unnecessary morbidity. [45] Current studies are focusing on this fact, with researchers requesting HPV-positive HNSCC to be classified as a separate disease entity. [1,7] The variation between treatment sensitivity is being investigated through efforts to understand the mechanisms behind increased response, as well as research to uncover optimal stratification of treatment. [22,63]

Indications of the future of HPV-positive HNSCC suggest that prophylactic vaccination against high risk genotypes of HPV will decrease the incidence of HPV-positive HNSCC; however, this will not be demonstrated for many years. [57] Current investigations are being conducted regarding the cost-effectiveness of vaccinating males. Some studies have suggested that vaccination would be beneficial, [64] whilst others have disputed this finding. [65] There exists a need to fully investigate this point. A large scale study is required and whilst it was not considered in the scope of this review, anal and penile cancers as well as the opportunity to reduce the incidence of benign HPV disease associated with HPV 6 and 11 need to be included in the economic evaluation. [14] Additionally, it may be useful to include the positive effect of herd immunity that vaccinating males would have, especially considering that some females will have sub-optimal immune responses. [57] Homosexual males also need to be considered in the evaluation. This study, which could be conducted in Australia, needs to be fully reported so that developing countries can assess HPV vaccination programs in males and females.

Conclusion

Much research has been conducted since the initial description of HPV and associated HNC development. The identification of the HPV oncoproteins E6 and E7 has allowed for the subsequent recognition of alteration in cellular pathways. The current treatment of patients diagnosed with HPV-positive HNSCC involves multi-disciplinary teams that often manage advanced disease with a positive prognostic status. Nonetheless, significant life-long treatment side-effects have been noted.

Future research is likely to focus on trials investigating the increased susceptibility of HPV-positive HNSCC to different treatment regimens and may include a classification of HPV-positive HNSCC as a distinct subclass of HNSCC with less aggressive treatment protocols. Prophylactic vaccination protection against high risk genotypes associated with HNSCC is expected to be fully investigated. This may include investigations of alternative methods of delivery.

It is essential that we capitalise on the current scientific development of prophylactic vaccines developed against HPV and actively educate parents of young children to vaccinate their children in order to avoid the complexities of HPV-positive HNSCC.

Conflict of Interest

None declared.

Acknowledgements

Thank you to Associate Professor Chris Perry, consultant in Otolaryngology-Head and Neck Surgery, Brisbane for allowing me to observe him in his role at the Head and Neck Cancer Clinic, Princess Alexandra Hospital, Queensland from which this review was inspired.

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Intra-vitreal bevacizumab in patients with Juvenile Vitelliform Dystrophy (Best Disease)

Dujon Fuzzard
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Dujon completed a Bachelor of Medical Science in 2009, conducting clinical research within a regional ophthalmology practice (Bendigo Eye Clinic). He grew up in Bendigo and is interested in pursuing a medical career within regional and rural Australia. Dujon's other interests include playing Australian Rules Football, athletics and playing the guitar.

Andrew is a Victorian-based ophthalmologist who grew up in Tasmania. After attending medical school in Hobart, Andrew completed his ophthalmic training at the Sydney Eye Hospital. To further his knowledge, he followed with a fellowship at the Royal Victorian Infirmary in Newcastle-Upon-Tyne in the United Kingdom. Andrew has practiced in a variety of locations throughout Victoria since the mid 1990s, including Footscray, Brighton, Shepparton and Bendigo. He is a Consultant at the Royal Victorian Eye and Ear Hospital, where he participates in the registrar surgical training programme. Andrew lives in Melbourne with his wife Tracey and three daughters.

Juvenile Vitelliform Dystrophy (Best disease) is a degenerative macular condition that is genetically inherited. In recent years monoclonal antibodies have been employed to help prevent the decline in vision associated with macular fluid. This report documents the use of intra-vitreal bevacizumab in two siblings (aged thirteen and fifteen) with Best Disease. This work studies the changes observed in visual acuity and macular oedema over a 39 and nineteen week period respectively.

Introduction

Juvenile Vitelliform Dystrophy (Best disease) is a rare genetic condition which damages the posterior pole of the eye over many years. It is caused by an abnormal *VMD2* gene located on the long arm of chromosome 11 [1] (11q12-q13) with inheritance via autosomal dominance. [2] A confident estimate of the incidence of this condition has not been made; however, due to its genetic nature, cases tend to appear in clusters. The largest sample of this sort has been found in Sweden, where 250 cases of Best disease were traced to a single (presumably homozygous) carrier who lived in the 17th century. [3] Afflicted individuals are initially asymptomatic, with a normal fovea and the only abnormality detectable present on electro-oculography (EOG). [4] The stages of Best disease are summarised in Table 1. Changes in visual acuity first occur usually between the ages of three and fifteen and coincide with the development of classic macular lesions of an egg-yolk ('vitelliform') appearance. Vision may remain stable from this point until a patient reaches their 40s, when acuity may decrease markedly. [5] Relatively recent developments in the use of monoclonal antibodies to reduce macular oedema may offer treatment benefits in this rare condition. In 2007, Leu *et al*. [6] reported functional and morphological improvement over six months in a patient of similar age treated for choroidal neovascularisation with intra-vitreal bevacizumab on the background of Best disease. However, other reports of patients being treated in this fashion are scarce.

Table 1. *Stages of Best Disease.*

Stage	Description
0 (Normal)	Normal visual acuity fundoscopic appearance. Abnormal EOG.
1 (Pre-vitelliform)	Pigment mottling of the macula. Visual acuity remains largely unaffected.
2 (Vitelliform)	Appears in early childhood. Features a round "egg-yolk" macular lesion. Visual acuity is mildly reduced (between 6/6 and 6/15).
3 (Pseudo-hypopyon)	Usually occurs during puberty. Part of the lesion is absorbed with minimal effect on visual acuity.
4 (Vitelliruptive)	Lesion atrophies and visual acuity reduces (to as low as 6/60).

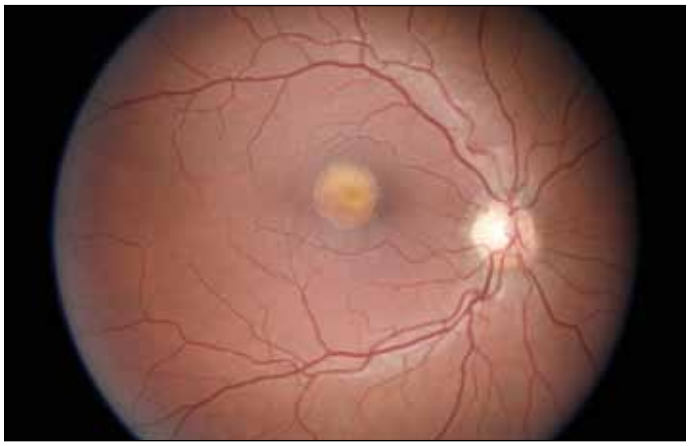

Figure 1. *Right fundus of Case One, eighteen months prior to the time of presentation with decreased left visual acuity. A vitelliform macular lesion typical of Best disease is present.*

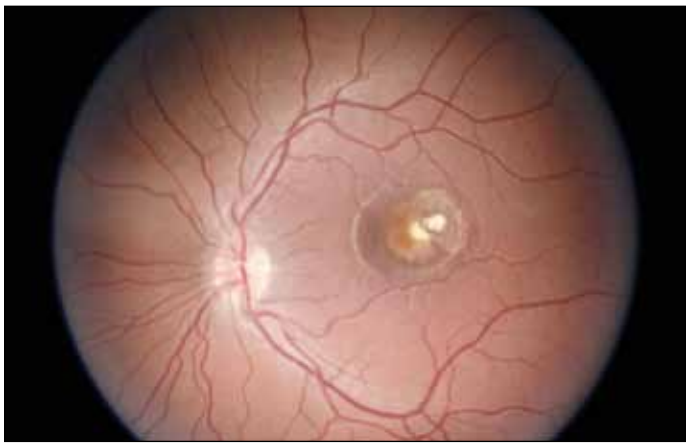

Figure 2. *Left fundus of Case One, eighteen months prior to time of presentation with decreased left visual acuity. A vitelliform macular lesion typical of Best disease is present.*

This work attempts to contribute additional information about the short term effects of bevacizumab when used for Best disease.

The Cases

The following report documents the effect of intra-vitreal bevacizumab on visual acuity and macular oedema in two siblings (aged thirteen and fifteen) with Best disease. Their father also has the condition and is legally blind. Informed consent to publish a report of the cases was obtained from the patients and their mother.

Case One

A thirteen year old male previously known to suffer from Best disease, stage two (Figures 1 and 2), presented eighteen months later with decreased left visual acuity. Fundus examination showed

classical bilateral vitelliform lesions as well signs of a left sub-retinal haemorrhage (Figures 3 and 4). This diagnosis was confirmed with fluorescein angiography (Figure 5) which also indicated the leakage of fluid within the vitelliform lesion.

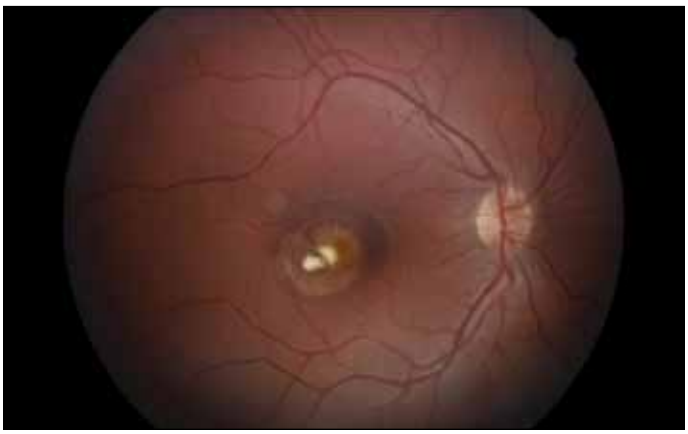

Figure 3. *Right fundus of Case One at the time of presentation with a vitelliform macular lesion.*

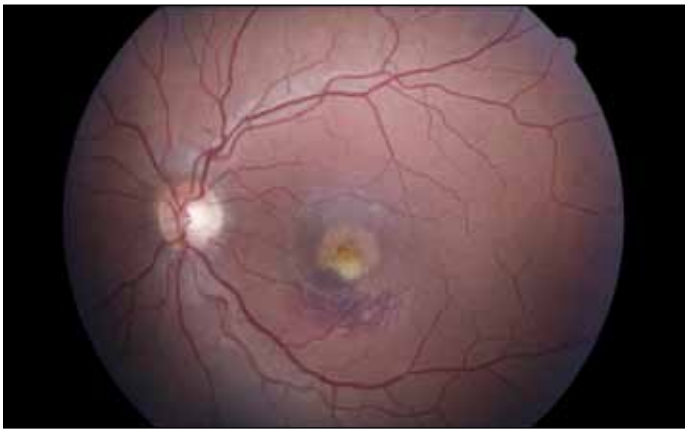

Figure 4. *Left fundus of Case One showing a classical vitelliform macular lesion with subretinal haemorrhage. Intra-vitreal bevacizumab was administered to the eye later on the same day.*

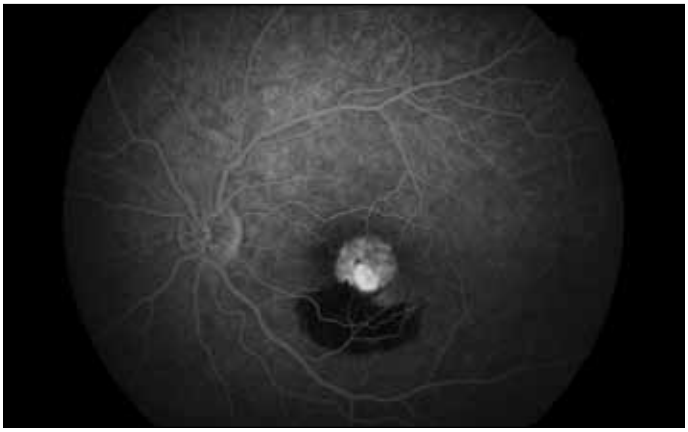

Figure 5. *Fluorescein angiography of the left fundus of Case One shows the presence of a sub-retinal haemorrhage (black region inferior to the fovea). Fluorescein dye is viewable in the overlying retinal blood vessels; however fluorescence is obscured from the choroid. By contrast, pooling of dye is evident within the vitelliform lesion.*

Comparison between examination findings at the time of presentation with fundus photos acquired eighteen months previously suggested the vitelliform lesions had become further advanced. Treatment of the left sub-retinal haemorrhage consisted of two doses of intra-vitreal bevacizumab (3mg/0.12ml per dose) administered to the left eye four weeks apart. The patient was observed through examination of visual acuity and spectral domain optical coherence tomography (SOCT Copernicus, Optopol S.A., Zawiercie, Poland). Eight weeks following the first bevacizumab treatment an improvement in visual acuity was observed. Furthermore, reduced macular oedema associated with the vitelliform lesion was also identified (Figures 6 and 7). In light of these improvements, intravitreal bevacizumab was subsequently administered to the right eye. Over a 39 week period of observation, visual acuity improved bilaterally (Table 2) despite the return of some macula oedema in the left eye (Figure 8).

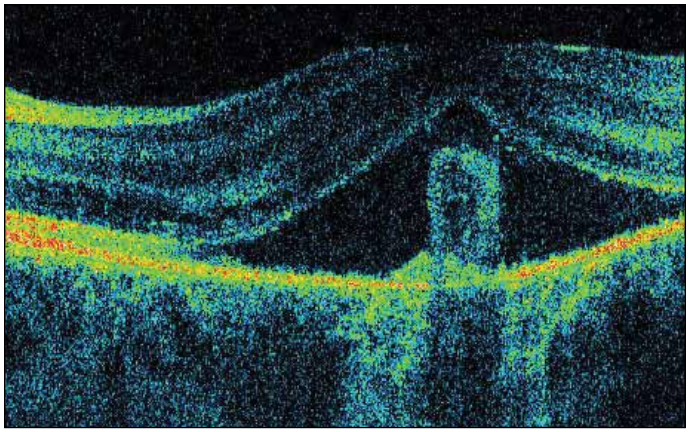

Figure 6. *OCT of the left fovea of Case One prior to administration of intra-vitreal bevacizumab shows the presence of macular oedema.*

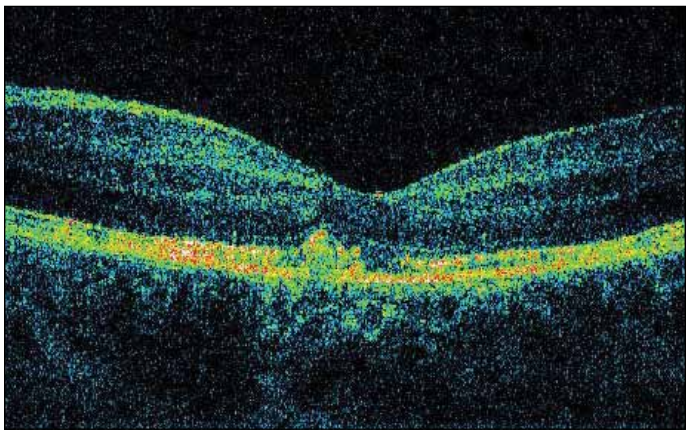

Figure 7. *OCT of left fovea eight weeks following initial bevacizumab treatment (Case One). Macula oedema is much reduced.*

Table 2. *Changes in visual acuity over 39 weeks in a thirteen year old male undergoing treatment for Best disease with intra-vitreal bevacizumab. At follow-up 39 weeks after the commencement of treatment, visual acuity has improved in both eyes.*

Weeks from date of first bevacizumab treatment	BCVA (right dye)	Right bevacizumab	BCVA (left eye)	Left bevacizumab
0	6/12+		6/9pt	#1
3	6/12all		6/12all	
4	6/12-		6/15-	#2
8	6/12-		6/7.5pt	
11	6/12pt		6/9.5+	
12	6/12+	#1	6/6pt	
16	6/9.5pt		6/6pt	
20	6/15pt		6/6pt	
23	6/9pt	#2	6/6-	
27	6/9pt		6/6-	
31	6/9.5pt		6/6all	
39	6/9.5pt		6/4.8-	

Legend: All BCVA (best-corrected visual acuity) measurements were recorded from Snellen and Bailey-Lovie visual acuity charts.

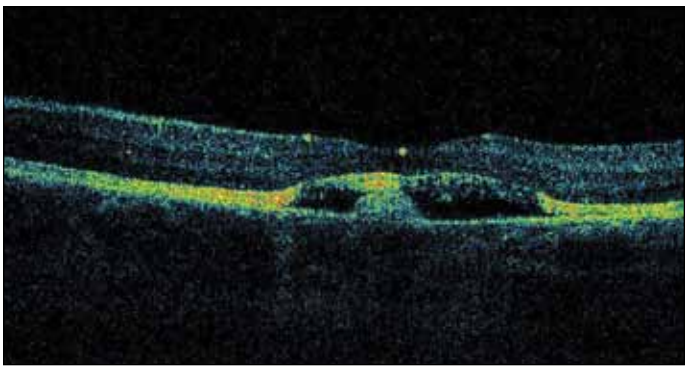

Figure 8. *OCT of left fovea 39 weeks following initial bevacizumab treatment (Case One). Some oedema is present, despite improved visual acuity. The lucent area under the neurosensory retina is due to the vitelliform lesion itself and may not indicate persisting choroidal neovascularisation.*

Cross-sectional view of the right macular on optical coherence tomography (OCT) remained relatively unchanged throughout the period of observation, despite a small improvement in right visual acuity (Figures 9 and 10). Further information regarding this case and initial follow-up of the intervention has been previously included in a scientific poster. [7]

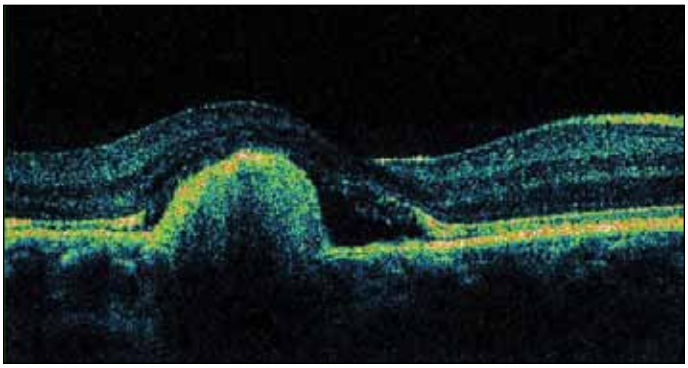

Figure 9. *OCT of right fovea of Case One prior to administration of intra-vitreal bevacizumab. There is evidence of macular oedema, as well a subretinal area of lucence likely to be due to the vitelliform lesion.*

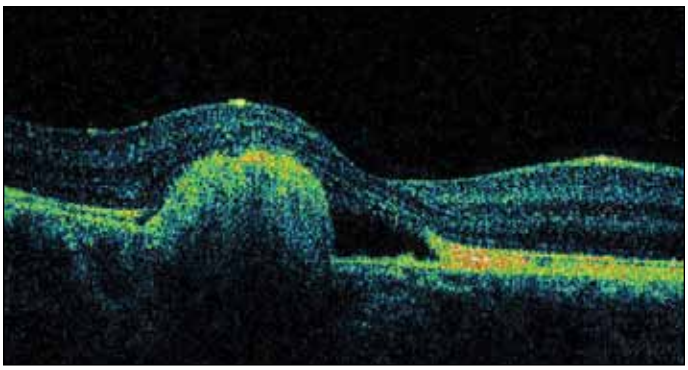

Figure 10. *OCT of right fovea of Case One, 27 weeks after initial administration of intra-vitreal bevacizumab. Compared with OCT acquired before treatment (Figure 9), a change in the level of oedema is not evident, despite a modest improvement in right visual acuity.*

Comparison with previous fundus photography (Figure 1) indicated that this lesion had progressed. Intra-vitreal bevacizumab was injected into this eye twelve weeks following the acquisition of this image.

Case Two

A fifteen year old female with Best disease (stage two) presented for review. Examination with OCT revealed the presence of bilateral macular oedema (Figures 11 and 12). Intra-vitreal bevacizumab was used in both eyes, initially in the right eye and three weeks subsequently in the left. Whilst minimal change was observed in the level of macular oedema four months after the initial injections (Figures 13 and 14) visual acuity showed a mild improvement (Table 3).

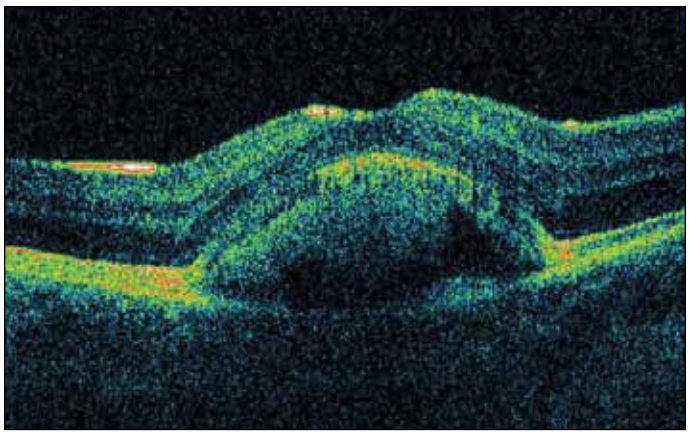

Figure 11. *OCT of right fovea of Case Two prior to administration of intra-vitreal bevacizumab. Macular oedema is evident, as is subretinal translucence suggesting the presence of a vitelliform lesion.*

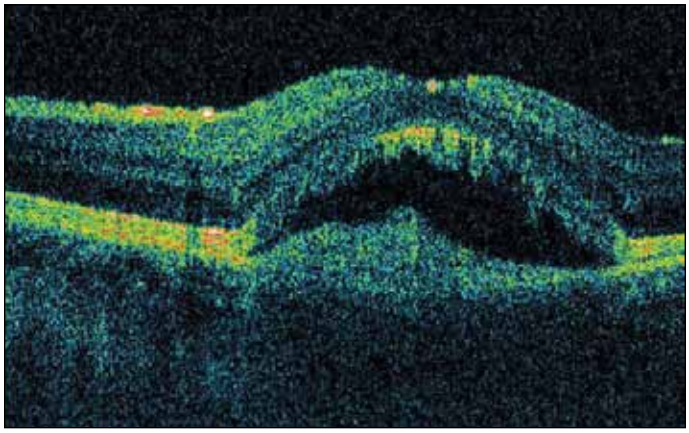

Figure 12. *OCT of left fovea of Case Two prior to administration of intra-vitreal bevacizumab. Macular oedema is evident, as is subretinal translucence suggesting the presence of a vitelliform lesion.*

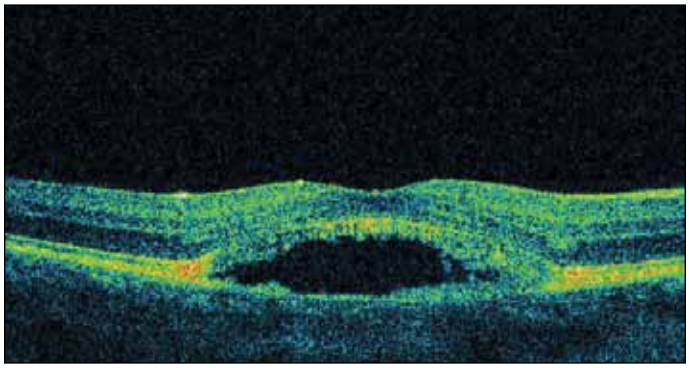

Figure 13. *OCT of right fovea of Case Two examined nineteen weeks after initial administration of intra-vitreal bevacizumab. Macular oedema remains present, despite an improvement in visual acuity.*

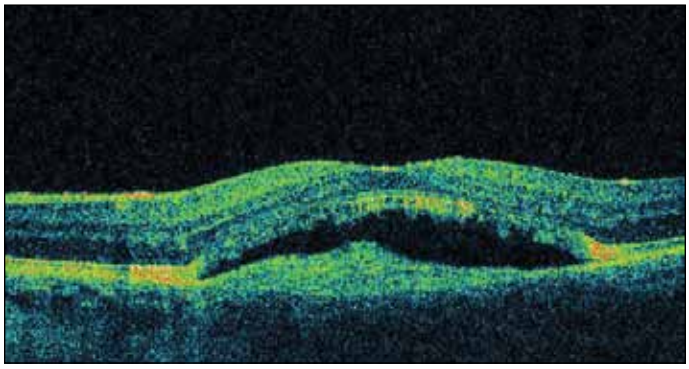

Figure 14. *OCT of right fovea of Case Two examined sixteen weeks after initial administration of intra-vitreal bevacizumab. Macular oedema remains present, despite an improvement in visual acuity.*

Table 3. *Changes in visual acuity over ninteen weeks in a fifteen year old female undergoing treatment for Best disease with intra-vitreal bevacizumab. Nineteen weeks after since the commencement of treatment, visual acuity has improved in both eyes.*

Weeks from date of first bevacizumab treatment	BCVA (right dye)	Right bevacizumab	BCVA (left eye)	Left bevacizumab
0	6/7.5all	#1	6/7.5all	
3	6/6pt		6/7.5+	#1
7	6/7.5all		6/7.5-	
11	6/6all		6/7.5-	
19	6/4.8-	#2	6/4.8pt	#2

Legend: All BCVA (best-corrected visual acuity) measurements were recorded from Snellen and Bailey-Lovie visual acuity charts.

Discussion

German Ophthalmologist, Franz Best, first described this hereditary condition in multiple members of a family in 1905. [8] Almost a century later, the identification of abnormalities of the *VMD2* gene (also referred to as *BEST1*) as the clear cause of the condition has provided clues as to why macular degeneration takes place in this patient group. It is known *VMD2* encodes for the trans-membrane protein bestrophin, which functions as a calcium-ion-dependant chloride channel within the retinal pigment epithelium. [9,10] Furthermore, additional work has shown that abnormal bestrophin protein forms malfunctioning calcium-ion-dependant chloride channels. [11] At present, the exact mechanism by which these abnormal channels produce the macular degeneration in Best disease is not fully understood. Existing hypotheses suggest that retinal pigment epithelial cells degenerate as a result of any one or more of abnormal cell volume, altered extra-cellular fluid composition or damage to cellular organelles from a changed ionic environment. [12]

Treatment of neovascular ('wet') macular degeneration with monoclonal antibodies such as bevacizumab (and also ranibizumab) has come about after the identification of vascular endothelial growth factor (VEGF) as a modulator of choroidal neovascularisation. [13,14] These monoclonal antibodies inhibit VEGF, thereby limiting the resultant oedema associated with poor quality neovascular capillaries. [15] To date, VEGF has not been identified as a contributing factor to the macular degeneration observed in Best disease. However, the altered cellular conditions resulting from abnormal calcium-ion-dependant chloride channels may indirectly provoke the localised release of VEGF. Determining the presence of high levels of VEGF in patients with Best disease would greatly further the case for management with monoclonal antibodies. However the answer to this question falls far beyond the bounds of this paper. Best lesions are not usually associated with choroidal neovascularisation. However these cases appear to have developed these complications. The relationship between these patients as siblings may have genetic significance.

A noteworthy topic is the use of OCT to monitor for macular changes during the treatment period. Previously, fluorescein angiography has been the primary investigation tool for monitoring the progression of macular oedema. [16, 17] However, OCT has been successfully used by previous workers [18,19] to observe the cross-sectional anatomy of affected eyes. Practical advantages of OCT use in these cases include the speed of image acquisition and lack of need for intravenous fluorescein. Whilst seemingly insignificant, these factors are noteworthy when repeated examinations are required in young patients.

The visual outcomes of the cases observed in this report suggest a temporary benefit of intra-vitreal bevacizumab in Best disease. In all four eyes of the two siblings treated, visual acuity showed at least mild improvement after four and nine months of follow-up respectively. Furthermore, a reduction in macular oedema was observed. That only two cases have been observed is a clear limitation to any conclusion. However, due to the extremely low incidence of Best disease, it is unlikely that trials of this therapy in this group of patients will ever be possible. Short term vision improvement is of particular benefit to young patients, such as the two cases in this report. Both patients are currently attending secondary school, where visual acuity needs are high.

From this work, it is impossible to determine whether long term benefits to visual acuity of patients with vitelliform macular lesions exist. Best disease has a poor visual prognosis, so a positive long term finding for any therapy would be welcomed with open arms by patients and clinicians alike. The critical issue to be addressed by future workers in this area pertains to whether increased levels of VEGF are present in the eyes of patients with Best disease. If found to be an effective treatment, determining the long term effects of intra-vitreal bevacizumab in this condition will require a concerted effort from the medical community, including longer term follow-up of visual acuity in larger numbers of patients.

Acknowledgements

Project facilitated by Mr Peter Burt.

Research conducted within Bendigo Eye Clinic.

Project feedback from Mr Robert Buttery.

Fundus photography by Ms Nerida Oberin and Ms Nicola Dehnert.

Conflict of interest

None declared.

Consent Declaration

Informed consent to publish a report of the cases (and relevant figures) was obtained from the patients and their mother.

Copyright

Information in this case report has not been previously published elsewhere, nor is it under submission for review with any other publishing organisation.

Correspondence

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IVC thrombosis: An unusual complication of metastatic prostate cancer

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Tim will shortly graduate from the Sydney campus of the University of Notre Dame Australia. He has varied interests in oncology, surgery and radiology. He also enjoys playing sport, riding his motorbike and fine dining.

This case report identifies an IVC thrombosis in a patient with stage IV prostate cancer. The case demonstrates hypercoagulability as one of the many complications of malignancy. The patient presented clinically with bilateral pitting oedema to the groin and into the scrotum with dilated superficial abdominal veins. The prostate cancer was aggressive and unresponsive to anti-androgen therapy and brachytherapy. The latest staging CT and bone scans revealed diffuse disseminated disease and a caval thrombus. He is now receiving chemotherapy as an outpatient and unfortunately his prognosis is unfavourable.

Case Introduction

Hypercoagulability is a known complication of malignancy and renal vein extension from renal cell carcinoma into the inferior vena cava (IVC) has also been extensively reported. However, IVC thrombosis (IVCT) is a rare complication of metastatic prostate cancer. Clinically, the venous obstruction presented with rapid onset bilateral pitting oedema extending to the groin. There were visible superficial abdominal veins. The swelling also caused pain and discomfort to the patient. The imaging appearances on ultrasound and computed tomography (CT) will be described in order to recognise this complication of malignancy.

Case Presentation

MA, a 57-year-old male retired nurse, presented to the medical oncology department with gross bilateral pitting oedema extending into the scrotum. The swelling began suddenly two days prior to his consultation.

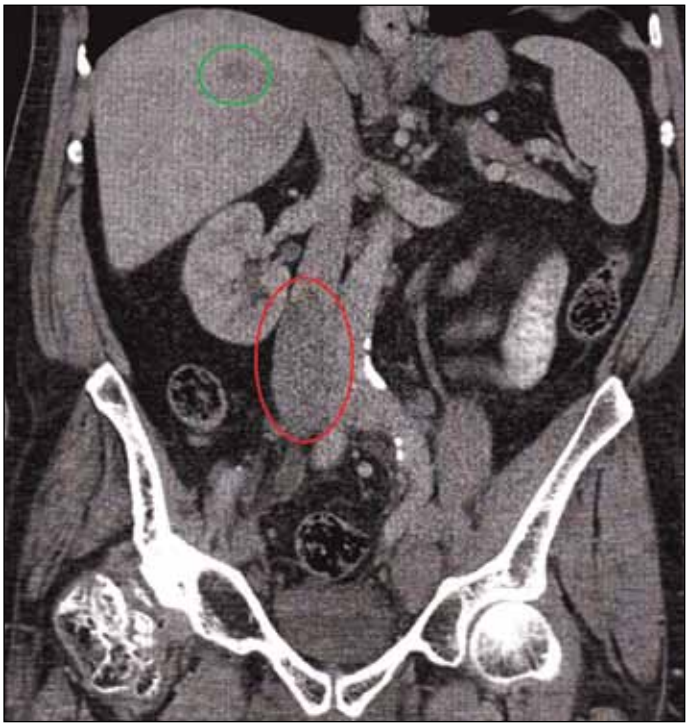

Figure 1. *Contrast enhanced abdominal CT scan: coronal section. This image demonstrates the ovoid hypodense filling defect in the IVC distal to the renal veins. The thrombus is expanding the cava (red circle). Note also the hypodense metastatic deposit in the liver (green circle).*

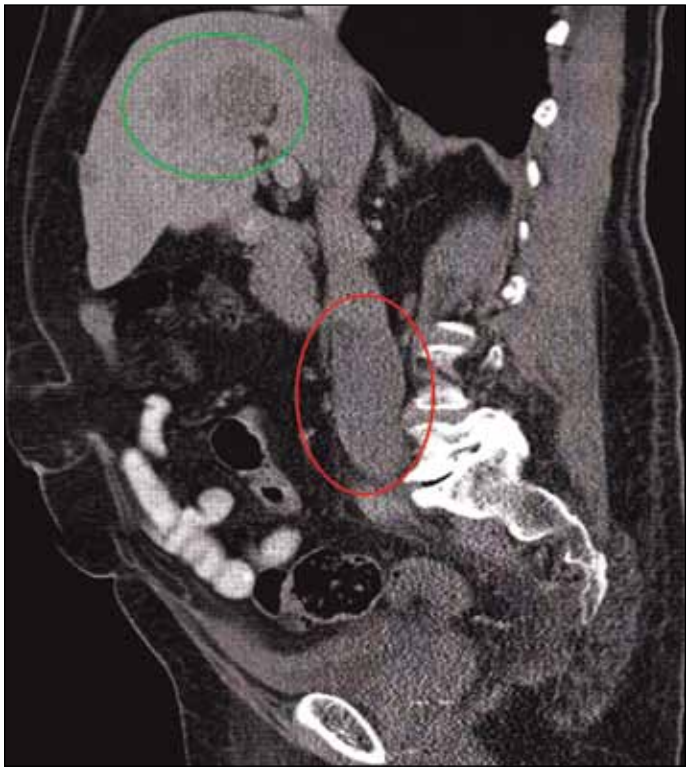

Figure 2. *Contrast enhanced abdominal CT scan: sagittal section. This image demonstrates the ovoid hypodense filling defect in the expanded infra-renal IVC (red circle). Note also the low attenuating metastatic deposits in the liver (green circle).*

The patient had a past medical history of non-Hodgkins lymphoma in 1992 and prostate cancer diagnosed in 2008. During this time he had experienced increased frequency, dysuria and poor urinary stream. His prostate cancer was diagnosed in 2009 after a PSA level of 7.2 ng/mL was found. Confirmatory prostate biopsy revealed high-grade adenocarcinoma with a Gleason score of 9. There were no obvious metastases found. He was treated with high dose brachytherapy to the prostate but despite this therapy his PSA continued to rise. In late 2010 his PSA had risen from 7 to 35.

A staging CT abdomen/pelvis and bone scan were performed at this time and showed only an enlarged prostate gland and degenerative changes in the lumbar spine and left hip. In 2011 the CT abdomen/pelvis and bone scans were repeated and revealed diffuse disseminated disease (stage IV). This included small nodules at the lung bases, extensive liver lesions and diffuse abdominal and pelvic lymphadenopathy. In addition, a caval thrombus was demonstrated (Figures 1 and 2) and confirmed with duplex Doppler ultrasound (Figure 3a). A direct comparison with a normal anechoic IVC in longitudinal section was also made (Figure 3b).

The thrombus was almost completely occlusive within the distal infrarenal IVC and extended into the right common iliac vein. Hepatic metastases and lymphadenopathy around the iliac vessels were again noted.

MA's medications included bicalutamide, leuprorelin, paracetamol, ibuprofen and oxycodone hydrochloride. He lived at home with his wife and was a non-drinker and non-smoker. There was no significant family history of malignancy.

On physical examination MA appeared well. His abdomen on inspection had distended superficial abdominal veins and was generally tender to palpation. There was bilateral pitting oedema to the groin extending into the scrotum. He was tender on palpitation over his lumbar spine. The remainder of the examination was unremarkable.

He received palliative radiotherapy at 20Gy in 5 fractions for metastatic deposits in the sacrum and lumbar spine and is currently receiving palliative chemotherapy with docetaxel every three weeks. His disease is incurable.

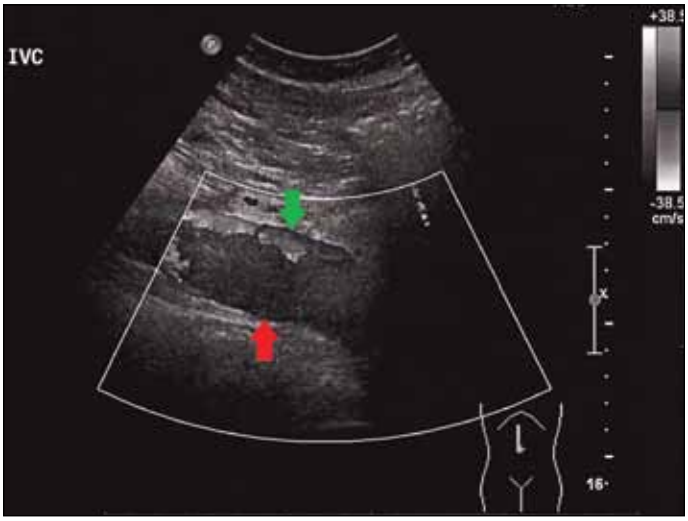

Figure 3a. *Duplex Doppler ultrasound: longitudinal section of the IVC. This image demonstrates the hypoechoic partially occlusive thrombus within the IVC (red arrow). There is some peripheral flow, most notably anterior to the thrombus (green arrow).*

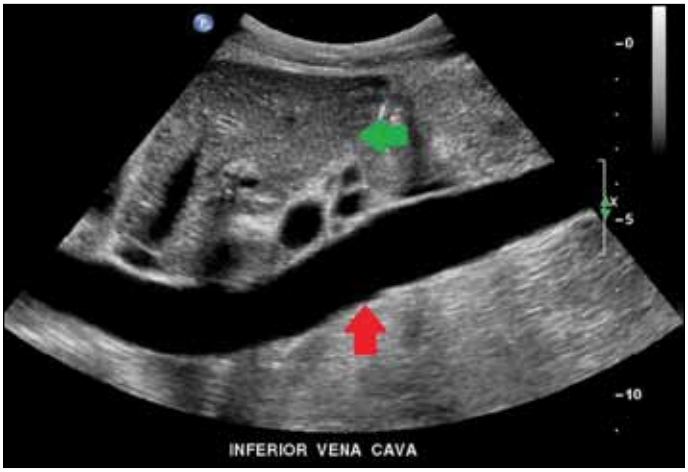

Figure 3b. *Ultrasound: longitudinal section of a normal IVC. Note the vessel is anechoic with no thrombus present (red arrow) posterior to the left lobe of the liver (green arrow).*

Discussion

IVCT is an under-recognised pathology and may develop from many conditions including malignancy. Whilst other causes exist such as trauma and a dysfunctional coagulation system, it should be noted that IVCT is frequently idiopathic. In Nepal it is endemic, with a suspected association with infections. [1]

Thrombotic disease has been reported in all types of malignancy especially with advanced disease. Patients with haematological malignancies such as acute leukaemia, lymphoma and multiple myeloma are also at high risk of thrombotic or haemorrhagic complications. [2] In a study by Ege *et al*., [3] the majority of thromboses in patients with malignancies were localised to the femoral vein (85.7%) rather than the IVC. Virchow's triad of stasis, hypercoagulability and vessel wall damage underpin the pathophysiology behind IVCT. [4] The combination of thrombosis and malignancy is also known as Trousseau syndrome. Notably Trousseau first appreciated this in 1865. [5]

The most familiar tumour linked with IVCT is renal cell carcinoma where the tumour directly invades the renal vein. Other reported tumours include teratomas and seminomas. Any tumours anatomically related to the IVC may result in direct compression causing stasis or turbulent blood flow, potentially inducing thrombosis. [4]

The pathogenesis of the hypercoagulable state in malignancy involves multiple variables. Intact tumour cells may express pro-coagulant activity that can directly induce thrombin generation; in addition, normal host tissues may express pro-coagulant activity in response to the tumour. [6] Expression of activated MET oncogene causes transformation of somatic cells and tumour growth. This may result in upregulation of PAI-1 and COX-2 resulting in inhibition of fibrinolysis and activation of platelets respectively. This interaction may lead to disseminated intravascular coagulopathy (DIC). [7]

IVCT may be treated medically or surgically and treatment is based on the underlying pathophysiology. Medically, therapy involves anticoagulation and thrombolytic therapy. In this patient, heparin was commenced immediately to decrease the risk of embolism. The merits of thrombolytic therapy must be weighed up against the risks of haemorrhage. Thrombolytic agents include streptokinase, urokinase and tPa. [4]

Used less frequently is surgical caval interruption and thrombectomy. Although caval filters allow central flow there is a risk of thrombus formation at the filter site. Re-thrombosis rates are significant with thrombectomy and the procedure usually does not remove the whole thrombus. Several interventional modalities are available to treat IVCT such as percutaneous balloon angioplasty, wall stents and Z stents. [4]

Conclusion

This case report outlines one of the rarer complications of malignancy. It is relevant as the prevalence of cancer within society is high.

Acknowledgements

I acknowledge Dr. David Dalley for his assistance and the images provided.

Conflict of interest

None declared.

Consent Declaration

Informed consent was obtained from the patient for publication of this case report and accompanying images.

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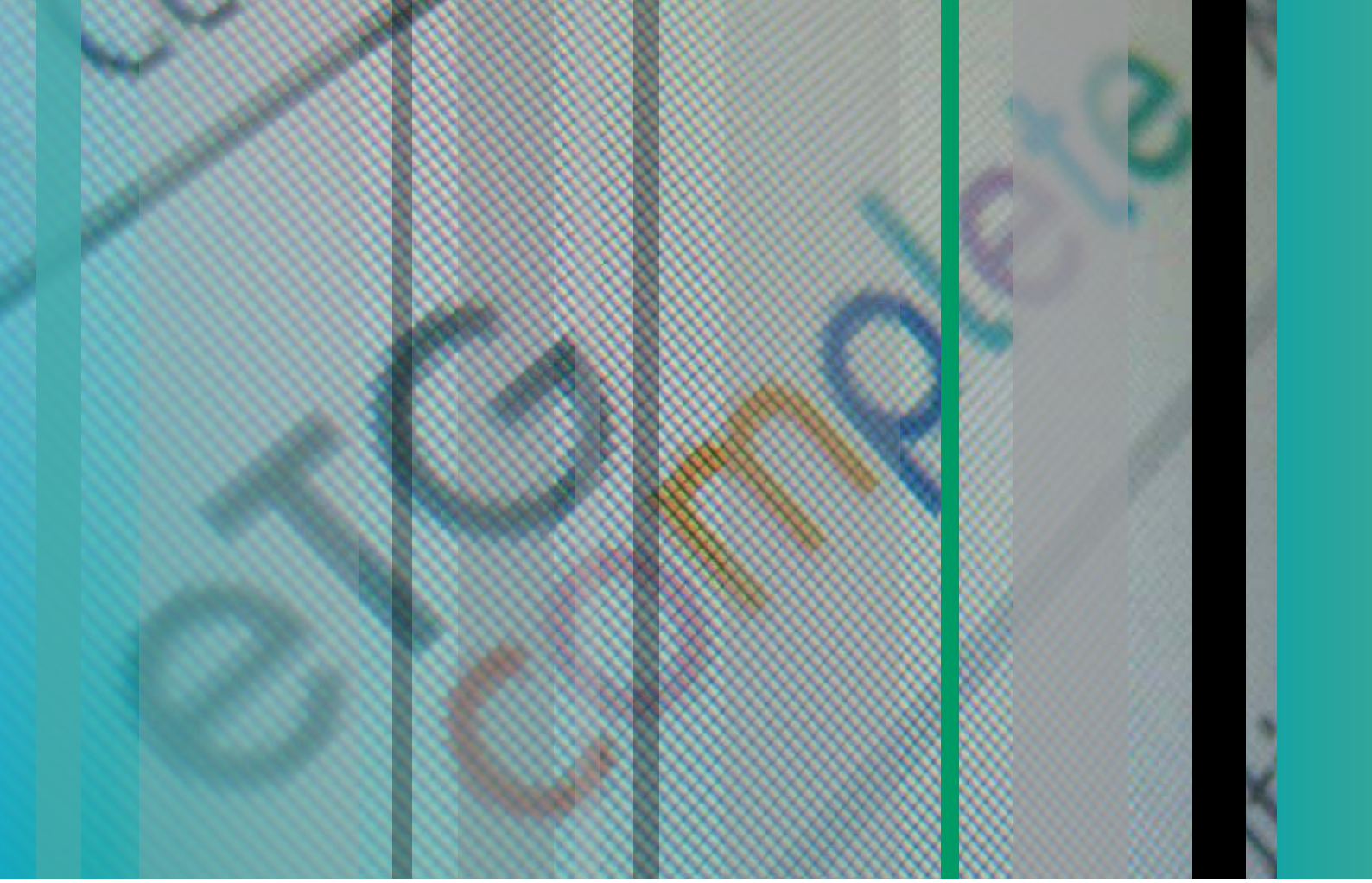

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Medical research at the cutting edge challenges society's closely held traditions

Prof. Alan Trounson
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Professor Trounson is President of the California Institute for Regenerative Medicine (CIRM) in San Francisco. Prior to joining CIRM in 2008, he was Professor of Stem Cell Sciences and Director of the Monash Immunology and Stem Cell Laboratories at Monash University, where he retains the title of Emeritus Professor. Professor Trounson founded the National Biotechnology Centre of Excellence or 'Australian Stem Cell Centre.' He has been a pioneer of human in vitro fertilisation and associated reproductive technologies; pre-implantation genetic diagnosis; as well as the discovery, production and use of human embryonic stem cells.

Introduction

I have had the experience of working in two major areas of human medicine that have been challenging and rewarding, and have provided some of the most heated debate on medical ethics and disturbance of established social mores. In many respects this made the developments even more difficult because they were frequently and avidly opposed by entrenched religious, political and gender advocates. The medical developments have been extremely successful. In the first place, human in vitro fertilisation (IVF) whose genesis occurred in the 1970s and 1980s has resulted in more than five million births worldwide and can no longer be simply quantified. In some countries with liberal health support systems, more than 3% of all live births are by IVF. The second great quantum development resides in stem cell based therapies, whose influence will be even more pervasive and influential, and whose significance is only just being evaluated in preclinical and clinical trials. This work has evolved from discoveries in bone marrow transplantation in the 1980s and 1990s and embryonic stem cell discoveries between 1998 and 2000.

Human IVF

Why should there have been so many problems in accepting developments that have such benefit to family and to health? In the first place, the moment of conception and first weeks of development were hidden and unable to be scrutinised or manipulated. They were the realms of deep significance in the Catholic religion and the province of control for some radical feminists. This led to strong criticism of IVF because conception was transferred to the laboratory predominantly under the influence of male researchers and clinicians. If the moment of conception is equated with personhood with the entitlement of the complete set of values of a born person, then IVF confers risks and issues that can be problematic. Freezing 4-cell to 100-cell (blastocyst) embryos in the first five to six days of development, their biopsy for inherited genetic disease and their disposal if they are not developing properly or are not required, become issues of conflict. They are, however, also the way in which infertile couples, and those with serious inherited genetic disease, can have a healthy family. Considerable efforts were made to prevent IVF from being provided to patients and even many social commentators decried the technology as being inappropriate as medicine and ineffective as a treatment. Clearly society has largely embraced IVF as an acceptable method of reproduction. Last year my friend and colleague, Robert Edwards, was awarded the Nobel Prize for Physiology for human IVF, a recognition after four decades of our research and medical applications.

Stem Cells

Since 2002, Australian scientists have been permitted to use donated IVF embryos in research. Under the Commonwealth legislation, Research Involving Human Embryos Act 2002, scientists can apply for a license from the National Health and Medical Research Council (NHMRC) to use donated human IVF embryos for stem cell research or research to improve infertility treatments and IVF, provided that the embryos are no longer required for infertility treatment. Additional legislation was also introduced in 2002, the Prohibition of Human Cloning Act 2002, which made it illegal to create, or even attempt to create, a human using cloning technology.

Prof. Alan Trounson

In 2005, the Australian legislation was reviewed by an independent committee which became known as the 'Lockhart Review' after the late Hon. John Lockhart AO QC who chaired the committee. The committee's recommendations were incorporated into legislation in 2006 following a conscience vote in both Houses of Parliament. The amended legislation – Prohibition of Human Cloning for Reproduction and the Regulation of Human Embryo Research Amendment Act 2006 – specifically allowed Australian researchers to apply for a license to use somatic cell nuclear transfer technology (SCNT, also known as therapeutic cloning) for stem cell research within a strict set of criteria. The amending legislation also increased the penalties associated with any attempts to abuse this technology to clone humans, with reproductive cloning remaining specifically prohibited. The legislation is currently being reviewed by an independent committee who were due to table a report on 27 May 2011.

James Thompson from Wisconsin and our own group at Monash University discovered human embryonic stem cells (ESCs) using methods pioneered by a friend and colleague, Martin Evans, who shared a Nobel Prize for this work. ESCs have the power of immortality and capacity to develop into any cell of the body (pluripotentiality). These characteristics provide these cells with an incredible potential for tissue repair and regeneration. The cells are derived from excess human embryos donated by IVF couples when they no longer wish to use their frozen embryos for reproductive purposes. This created another major social dilemma because the embryos were used

for research and potential therapeutics rather than reproductive purposes. There have been numerous committees formed to protect the sanctity of these donated embryos although patients are permitted to discard (destroy) them if they wish. In the USA, President George W. Bush forbade any further derivation of ESCs with federal funding and President Obama overturned this. Nevertheless, a District Court judge of the District of Columbia found in favour of two scientists who claimed the federal funding of embryonic stem cell research was illegal because of the Dickey-Wicker Amendment, which is usually attached to US budget bills. This was despite President Bush's Administration's prior support of limited research on embryonic stem cells with federal funds. Presently the decision is in appeal but federal funding has all but ceased for new studies.

Is this motivated by ideology and religion? The plaintiffs who brought the action were certainly of this philosophy. The courts are generally conservative but perhaps the appeal will succeed. In the meantime, California raised US$3billion for stem cell research during the Bush Presidency (2004) and as President of this organisation, I am able to support the groundbreaking research that is taking stem discoveries to the clinic for the potential treatment of spinal injury, macular degeneration, type I diabetes, a cure for HIV/AIDS, destruction of inoperable gliobastoma, leukaemias, other solid tumours, inherited sickle cell anaemia, epidermolysis bullosa, stroke and amyotrophic lateral sclerosis (ALS).

Although the roots of ALS are uncertain, three genetic mutations have been linked to it. Researchers had to determine just where the mutations did their dirty work. Were motor neurons damaged by their own genes, or was the damage caused by gene expression in neighbouring cells? The symptoms of ALS appear when motor neurons detach from the muscles they innervate. Using rodents genetically engineered to develop ALS, Dr. Don Cleveland and his team at the University of California, San Diego School of Medicine, first shut off the ALS gene in the motor neurons, but kept it running everywhere else. As expected, the onset of disease was delayed, but there was little meaningful improvement.

The researchers then reversed the experiment, keeping the gene going in the motor neurons, but shutting down its operation in their 'intimate partners', astrocytes. In this case, symptom onset was unchanged, but the disease's progression slowed dramatically. It appears astrocytes with the ALS mutation release a toxin that damages the motor neurons. The animals ended up living twice as long and the team hopes to replace mutant-expressing astrocytes with normal ones in ALS patients.

Life Technologies Corporation of Carlsbad, California, is growing embryonic stem cells and coaxing them to become astrocyte precursor cells that will then be injected into the spinal cords of ALS patients. That trial will begin within four years if animal trials succeed.

Huntington's disease is another affliction that is the target of stem cell researchers. Some 2,000 people are diagnosed with Huntington's every year in the United States. Unlike many inherited diseases, which require two copies of a disease-causing gene to wreak havoc, Huntington's, an autosomal dominant disease, rears its head with a single mutant gene. Therefore, offspring of those with Huntington's have a 50-50 chance of developing the always-fatal disease. In this disease mesenchymal stem cells move from brain cell to brain cell, looking for the injured.

Dr Jan Nolta, Director of the University of California Davis Institute for Regenerative Cures, intends to harness the paramedic services of these bone marrow–derived cells and treat Huntington's disease. Inserted into the brain, these cells actually seek out damage. The errant Huntington's gene is a copy machine run amok, repeating the recipe for the same three nucleic acids 38 times or more. The protein created by this wild repetition, called huntingtin or htt, damages a class of brain cells called medium spiny neurons.

When a medium spiny neuron is healthy, it is shaped something like a spider web, with axons extending in all directions, controlling movement, cognition and emotion. But under huntingtin's influence, it pulls in those axons. Cell-to-cell communication stops, and the person develops involuntary dance-like movements, known as chorea. The condition leads to behaviour changes; a sweet-tempered person becomes irascible. Cognitive function also declines.

To disrupt this destruction, Nolta married the mesenchymal cell's charitable tendencies with a huntingtin-killer. On their own, mesenchymal cells secrete neural growth factors that can restore synaptic connections, though they cannot touch the huntingtin, which continues to plunder. Animal studies, however, showed that strands of RNA can be tailored to cleave the huntingtin RNA, decreasing Huntington's symptoms and prolonging survival. Nolta's team of researchers engineered mesenchymal stem cells to manufacture short interfering RNA, or siRNA. Videos of mesenchymal cells engineered to make this siRNA show cells pouring the siRNA into any sick cells they encounter. Her team has a patent pending on this technology.

The first human studies will use the mesenchymal cells without siRNA, to study the effect of the neural growth factors that mesenchymal stem cells produce. The next study will add the siRNA to the mesenchymal cells.

So how does the balance of potential merit verse ideology influence society in support of new cell based therapies? The community in the US is now 70% supportive of ESCs across all ages and religions. In addition, induced pluripotent stem cells (iPSCs) have been created by Dr. S. Yamanaka using the integration of four transcription factors into adult skin and other cells that solves the ethical dilemma about using ESCs. This was developed on the knowledge of transcription factor activity in human ESCs and provides another incredible new platform for the interrogation of human disease and potential applications in regenerative and personalised medicine. I expect my friends Shinya Yamanaka and John Gurdon (frog nuclear transfer) are likely to win a Nobel Prize for their work on reprogramming cells.

I have had a wonderful career as a research scientist and couldn't have wished for a more fulfilling life. Perhaps some of you will become interested in making new contributions in science and medicine. If you want to make major changes to the status quo, be brave and be prepared for the challenges for interfering with society's closely held traditions.

‘We want you to be our mother’: Research to improve Aboriginal child health

Prof. Fiona Stanley
Director, Telethon Institute for Child Health Research

Named Australian of the Year in 2003, Professor Stanley is a vocal advocate for the needs of children and their families. She is the founding Director of the Telethon Institute for Child Health Research, a multi-disciplinary centre conducting research into the prevention of major childhood illnesses. She is a Professor in the School of Paediatrics and Child Health at the University of Western Australia, and the Chair of the Australian Research Alliance for Children and Youth. In 2004, Professor Stanley was honoured as a “National Living Treasure” by the National Trust. She is the UNICEF Australia Ambassador for Early Childhood Development and has served on the Prime Minister’s Science, Engineering and Innovation Council (PMSEIC) for several years.

Surely we don’t need any more research? Surely we know what to do to improve Aboriginal health? Surely we know the best environments for healthy child development? In this article I provide a rationale for Aboriginal child health research, give a history of my own personal journey in Aboriginal child health from the 1970s to 2011, give examples of our research and its application to improve outcomes and how we have provided the environment to build the careers of Aboriginal researchers; and finally, end with several recommendations.

The aims of the Telethon Institute for Child Health Research (TICHR) are fourfold:

1. To conduct high quality research;
2. To apply research findings (not only our own) to improve the health and well being of children, adolescents and families;
3. To teach the next generation of health researchers; and
4. To be an advocate for children, for research and for social justice.

We do all this by working in groups across themes of major childhood diseases and problems, including all areas from genes and cells, to children and families, to population-wide influences. Hence we have basic, clinical and population sciences all working together to investigate causal pathways, discover better treatments and to apply new knowledge wherever we can. We provide an enhancing research environment with excellent research support – including access to data, data management and analysis, bioinformatics, consumer and community participation and encourage a culture of communication both internally and to the external world (for example, media training).

National and international collaborations are essential for any research, particularly in Australia where we have small sample sizes and are a long way from conferences and other research environments. Perth is said to be isolated, but every day in our Institute people are working with other researchers from many different countries and parts of Australia (from Papua New Guinea to New York City; from Kununurra to Cairns). Such collaborations are increasingly exciting and useful for our increasing group of Aboriginal scholars.

Rationale for Aboriginal research

The very disparate circumstances facing Aboriginal Australians compared with non-Aboriginal Australia highlight the need to ‘close the gap.’ [1] The most recent estimates from the Australian Bureau of Statistics (ABS) indicate that an Aboriginal male born in the period 2005-2007 could be expected to live to 67.2 years, approximately 11.5 years less than a non-Indigenous male at that time. In the same period, an Indigenous female could be expected to live to 72.9 years, which is almost 10 years less than a non-Indigenous woman. [2]

The gap is huge; when we merge these high death rates in young adults with the population pyramids (Figure 1) which show the relative youth of the Indigenous population, 50% aged less than twenty years, it is clear how this impacts on the human capability of Aboriginal society generally. [3]

For example, this demographic pattern means that for every Aboriginal child there are only 1.19 adults, in comparison with nearly three adults for each non-Aboriginal child. If the adults are also sick or

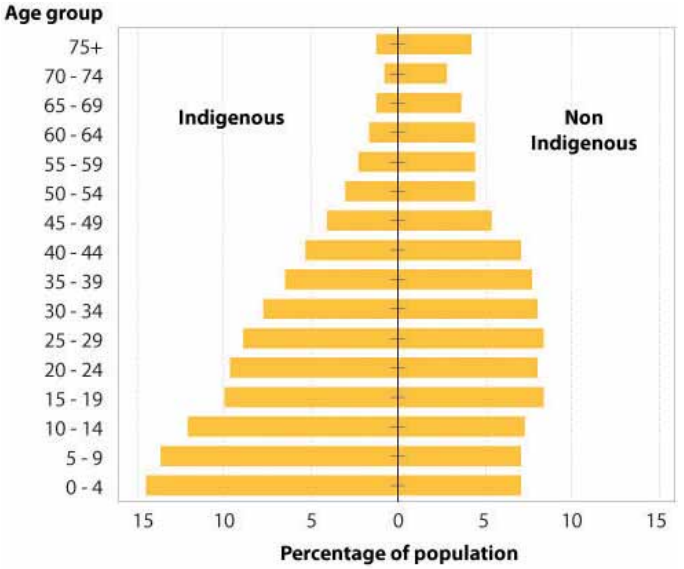

Figure 1. *Population pyramid demonstrating the relative youth of Australia’s Indigenous population, 2009. [4]*

compromised, the environment that they can provide for the care and welfare of their children is limited, as is their capacity to participate in the work force, in education or use services effectively. This is important for us to understand as if our policies and practices are developed from non-Aboriginal constructs and assumptions, then we, as health professionals, will continue to fail our Aboriginal brothers and sisters.

Figure 2 illustrates the very clear pathways from colonisation to today’s problems in health, such as infections, cardiovascular disease and diabetes and in social areas, such as domestic violence, child maltreatment and substance abuse.

Anyone providing services in health, education, child protection, housing or justice must appreciate these pathways. To ignore them

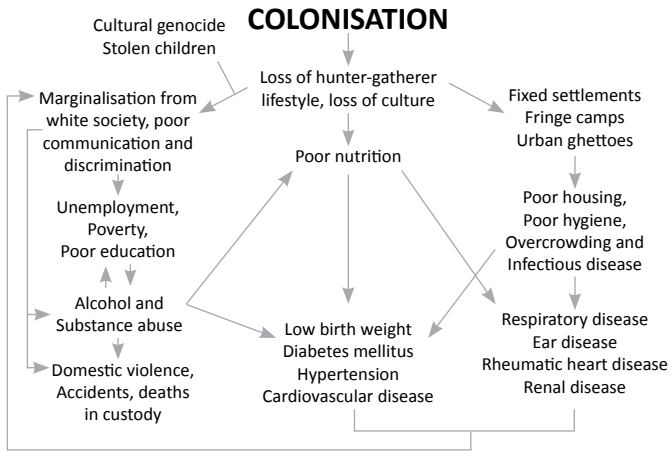

Figure 2. *Flow diagram showing the relationship between colonisation and health today. [5]*

and focus on the end of the pathways to provide crisis care will never result in reductions in these problems and could actually increase them. For example, by providing renal dialysis in remote locations we will keep people alive for longer, but will never reduce the incidence of renal disease. And by ignoring the cultural, social, emotional and environmental pathways to this range of problems, our solutions will not only be too late – they will be focused on singular factors and hence, will again be less effective.

Thus the rationale for continued research to improve health and wellbeing is that whilst we have done some useful research (particularly in vaccines and other population-based interventions), we have failed hugely to implement effective services to improve outcomes for Aboriginal people. This is not only in health services – with the gap in mortality but one measure – but in all other social and welfare services. The considerable waste of money, time and people in delivering ineffective services should be our biggest shame. [6] So, the answers to my initial questions are clear: we do know what to do, but we do not know how to do it. We appear to have ignored the very people with whom we need to work most closely – the Aboriginal people themselves.

History of Aboriginal health research in Western Australia

I commenced working in Aboriginal health in the early 1970s by joining the Aboriginal Advancement Council in East Perth, working in the paediatric Aboriginal Clinic. I also conducted two state-wide surveys to look at living conditions and health status outside of the metropolitan area. This started me on a road to work in epidemiology and public health, as I realised that prevention of disease in children was the best way for me to practise medicine.

I trained overseas in the UK and USA and returned to Western Australia (WA) in the late 1970s to establish the first Australian group in perinatal and paediatric epidemiology and preventive medicine. This involved creating population disease data collections and linking them together to identify Aboriginal status – in those days neither birth records nor death certificates had Indigenous identification. To obtain death and disease rates for Aboriginal mothers and children, we expanded the Midwives Notifications of Births to include race and other variables and produced Australia's first comparative Maternal and Child Health (MCH) statistics. At the same time, in 1984, we appointed our first Aboriginal health researchers, Gloria Walley and Patricia Morich, and developed a dedicated team to work on the Aboriginal MCH data.

In the 1990s we all moved in to the new Institute for Child Health Research, which I established on the campus of the Princess Margaret Hospital for Children. This decade signalled two major changes in our work – we started working directly with Aboriginal communities (rather than just looking at their data, but of course we continued to do that too); and we, with the guidance of our Aboriginal partners, developed acceptable cultural research practices. [7] With a group of Aboriginal women in the Eastern Goldfields and with National Health and Medical Research Council (NHMRC) funding, we set up a MCH model service run by Aboriginal health workers. Ngunytji Tjitji Pirni, which means 'mothers and grandmothers working together' in Wongai, is still going seventeen years later as an incorporated organisation with many of the clients now working in the service themselves to deliver more acceptable care.

The first project in Australia with an Aboriginal chief investigator (Indigenous medical graduate Dr. Sandra Eades, a Nyoongar woman) was also conducted in the 1990s, called Bibbulung Gnarneep ('solid kid' in Nyoongar). It was an urban cohort study investigating the major influences on pathways from birth to a range of health outcomes. [8] From this decade we had started on a road to develop Aboriginal researchers to run their own agenda, become research leaders and to work more effectively with us on projects that they developed and with methods they knew were respectful and acceptable. Dr. Eades was the first Aboriginal medical graduate in Australia to be awarded a PhD, in 2004.

In the 1990s, Dr. Eades and I went to local Aboriginal leaders with Ted Wilkes (Head of Perth Aboriginal Health Service) and asked them the question: 'We are a research institute and not a service provider; here is what we have done and are doing now – what do you want us to be?' They responded, 'We want you to be our mother.' Mothers, they explained to me, give birth to their children, give them all the love, nurturing, advice and capacity/education to prepare them for life and then let them go (but are always there for them). This was a clear call – help us get research skills and 'know-how' (how to win grants, write papers, translate findings, advocate with data and so on) and then relinquish the responsibility and capacity to us. Hence, Kulunga was born, a joint venture between our Institute and the Aboriginal-controlled health organisations in WA. Kulunga's aims were to grow Aboriginal research capacity, conduct the most important, relevant and culturally appropriate research with Aboriginal partners and assist them to translate this to improve outcomes. Specifically, Kulunga's vision is to:

- Develop a network which enables Aboriginal people to conduct research and training, which will form the basis for improvement in health and whole life expectations for Aboriginal children and families in Western Australia.
- Kulunga respects the right of Aboriginal people to control research activities in keeping with the principle of Aboriginal self-determination.

It has been a fabulous, if challenging, path.

Throughout the 2000s our Aboriginal research agenda in TICHR has expanded enormously, as have the numbers and capacity of our Aboriginal researchers. Aboriginal research projects have been conducted in a range of areas, including mental health, child development, education, infectious diseases (particularly otitis media), birth defects such as neural tube defects and fetal alcohol syndrome, and interventions such as swimming pools in remote communities, early parenting programs and surveys to influence policy and practice.

The first workshop to develop an NHMRC roadmap for Aboriginal health was run out of TICHR and resulted in more support from the NHMRC for Aboriginal research and researchers nationally. [9] We were awarded the first Aboriginal NHMRC capacity building grant with all of our ten team investigators being Aboriginal. They were Cheryl Kickett-Tucker, Ted Wilkes, Helen Milroy, Jan Hammill, Dawn Bessarab, Daniel McAullay, Juli Coffin, Dr. Ngaire Brown, Dr. Sandra Eades and Dr. Michael Wright, who met with Sir Richard Doll on the first day of the grant.

All of these investigators now have their PhDs (except Professor Ted Wilkes whose work on high level national committees has precluded him working full time in research). All have now gone on to post-doctoral fellowships and research and are winning grants as Chief Investigators. One such grant, awarded in 2010, is our Centre for Research Excellence (again NHMRC) which asks two simple questions: 'Why do services fail Aboriginal people?'; and 'What works and why?' Of the ten Chief Investigators, eight are post-doctoral Aboriginal researchers dedicated to answering these questions using a range of different approaches. These include cultural competency, community engagement and community participation action research – powerful and empowering methods to fully engage the people for whom the services are meant. Much of this work comes up against racism, bureaucratic silos and inertia, vested interests, apathy and sheer ignorance by mainstream providers of the Aboriginal population and their circumstances.

Whilst I could give many examples of our research, space limits me to a few. One project conducted by us was the WA Aboriginal Child Health Survey (WAACHS) – the most comprehensive survey of Aboriginal child and youth health, education and family circumstances ever done in Australia. [10-13]

For those who deny that the 'stolen generation' actually occurred, Figure 3 shows the extent of forced removals in today's WA families.

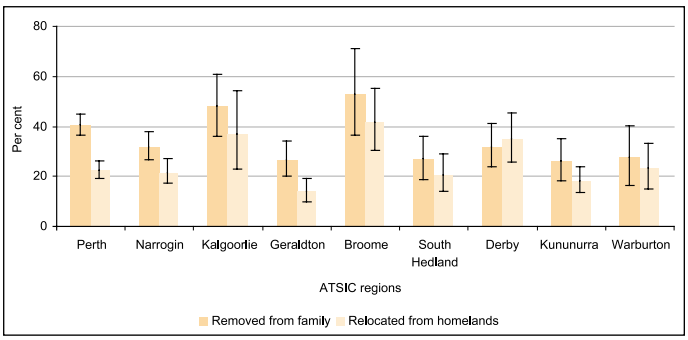

Figure 3. *Percentage of Western Australian children living in a household affected by forced separation or relocation 2000-2001. [14]*

The results of the WAACHS demonstrated that children with a primary carer who was forcibly separated from their natural family as part of government policy were more likely to:

- Be at higher risk of clinically significant emotional symptoms (30.7 percent; CI: 24.9%–37.1%) than children looked after by primary carers who were not forcibly separated (20.7 percent; CI: 18.4%–23.1%);
- Be at higher risk of clinically significant conduct problems (41.5 percent; CI: 35.0%–48.4%) than children looked after by primary carers who were not forcibly separated (31.8 percent; CI: 29.3%–34.4%); and
- Have a higher mean conduct problems score (3.24; CI: 2.89–3.59) than children looked after by primary carers who were not forcibly separated (2.65; CI: 2.51–2.79); [15]
- Thus, showing inter-generational impact.

The four volumes of the WAACHS have been influential across all Australian states and territories in terms of policy and approaches to prevention of child and youth problems.

Our swimming pool studies in two remote WA communities were carried out over six years and demonstrated dramatic improvements in health (skin infections, ear disease and antibiotic usage), school attendance and self-esteem. [16,17] This has resulted in swimming pools being built in many more communities around Australia with similar impacts on health status.

Finally, there are several recommendations that I would suggest to those who want to influence this important area in Australia. All of us, as medically trained people, should be across these issues even if not directly involved with Aboriginal people because it is totally unacceptable that a wealthy and capable nation like Australia has such an unacceptable gap in health and well being outcomes within its society.

Recommendations

1. Develop a Reconciliation Action Plan for your organisation: this should be a living and changing document to acknowledge Aboriginal Australia, partner with Aboriginal people and fulfil our collective responsibilities to our nation's first people.

2. Employ Aboriginal people wherever possible: it might even be worth having a policy to engage in this way as we do for gender balance and to avoid discrimination. Some states in the USA measure racism by collecting data to see whether the employment of certain racial groups matches their proportions in the populations of those areas. We could do the same here – some organisations such as Australia Post have had an Aboriginal employment policy for years with success all over the nation.

3. Build Aboriginal capacity: so many Aboriginal projects and programs are set up to fail because they do not help/train/support Aboriginal people to develop the range of skills needed to succeed in a tough dominant culture with many harsh features and barriers to success. Our experience in building an Aboriginal health research capacity has been a two-way process with many of us learning better ways of doing our research and viewing pathways to health and disease in more holistic ways. Health and welfare services should be full of competent and confident Aboriginal people, fully trained to tackle the complex issues which face them.

4. We need to change our focus from researching the pathways into poor outcomes, to researching success: that is, why so many Aboriginal children in high risk situations do so well is more helpful to know than why so many of them do so poorly? If we want to make a positive difference then knowing success pathways is the way to go.

5. Advocate for Aboriginal people: do this with them, with respect and do not give up. Having data is very powerful for advocacy because if collected and analysed well it cannot really be ignored.

6. We must work with Aboriginal people to ensure that services of all kinds are culturally acceptable, that staff are culturally trained and competent; and that they are aware of the very negative effects of racism on use and effectiveness of services and how real and powerful they are on individual and collective self esteem.

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How fortunate we are

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Laurel Imhoff is an enthusiastic general surgery resident committed to evidence based practices. During medical school she was captivated by the operating room and the personal rewards of the surgical "hands on" approach to disease. She began a general surgery residency at the University of California at San Francisco-East Bay Program in 2007 where she is currently training today. Her long-term mission is to make a lasting difference in the lives of her patients by providing excellent and compassionate surgical care and to influence surgical practices with skilful outcomes based clinical research.

Professor Alden Harken has been the Chairman of the Department of Surgery at UCSF-East Bay for 28 years. He also served as a Regent of the American College of Surgeons for nine years; but, he is proudest of the teaching awards that he has received at each of the three universities in which he has served on the faculty.

As students of medicine, you will soon be educationally unique – with a body of knowledge that no one can ever take away from you.

When you receive your MBBS, the society and community in which you live is making a statement of trust in your abilities. With that trust you will be afforded extraordinary privileges and esteem. However, with the esteem and privilege comes the heavy responsibility of your patients' well-being. You are all remarkably capable – and, remarkably fortunate to be so capable.

John Adams, the second president of the United States, observed: "The luckiest people in the world are those who are doing something that they think is important, and that everyone else thinks is important." As physicians, we are fortunate to be guaranteed an intellectually stimulating, socially gratifying and comfortable life. These luxuries, however, come with the price tag of responsibility. Those of you who treat individual patients – and make them better – will be rewarded. I encourage you as physicians, however, to reach out into your communities and use your position to identify and solve social problems. I will argue that primary school education, teen pregnancy, high school dropout rates and homelessness all have healthcare ramifications. As a physician, it will be simple, gratifying and rewarding to identify these problems and to get involved. Marion Wright Edelman noted: "Service is the rent we pay for living; it is the very purpose of life and not just something you do in your spare time."

There is the story of a physician standing beside a river. A body floats by, face down. The physician dives in, drags the guy out, performs CPR and resuscitates him. Our physician returns to the riverbank, and another body floats by. Our hero dives in again and rescues and resuscitates the victim. He returns to the riverbank and another and then another body floats by. Our physician is socially and intellectually responsible, to go to the river's origin and inquire: "Hey, what's going on here?" We have a moral obligation to identify the root cause of problems, and take preventive action rather than being reactionary.

Dr. Laurel Imhoff

Prof. Alden H. Harken

We live in an age that believes in the progress of science. Prior to the Enlightenment, however, it wasn't always that way. In 399 BCE, Socrates was put to death in "liberal" Athens, the birthplace of democracy, for corrupting young minds and disbelief in the gods of the state. In the 1600s Galileo was persecuted for promoting the heliocentric view that the sun, not the earth, was the center of the universe. The advancement of thought and science was stifled by those in power.

Then in the eighteenth century, the French Enlightenment replaced the ancient ideology of cyclic pessimism with the modern concept of inexorable scientific advance. Voltaire, who personified this transition, proclaimed: "…that reason and human industry will always continue to make progress." This optimism continued when the 20th century American philosopher, John Rawls, proclaimed in his enormously influential book, *A Theory of Justice*, that we are all motivated by what he identified as an "Aristotelian Principle." He stated: "…that human beings enjoy the exercise of their realised capacities (your innate or trained abilities) – and, this enjoyment increases the more the capacity is realised, and the greater its complexity." The intuitive idea here is that we all take more pleasure in doing something directly as that activity becomes more complex and as we become more proficient at it. In medicine, you will encounter an essentially unlimited opportunity to improve and as you master medicine's intellectual and psychological challenges you will derive immense gratification.

We physicians straddle the divide between the physical and metaphysical worlds. Scientific medical knowledge is progressing at a dazzling rate – it is supposed to be doubling every decade. The most

successful among you will be welcomed into the innermost sanctum of our patients' lives and be spiritually, socially and even legally empowered to use a full bag of pharmacological, psychological and even spiritual tools to make your patients "feel better" and that is our goal: to make our patients "feel better." And, we hope you will also reach out into the communities in which you serve and inquire, "Hey, what's going on up at the headwaters of this river?"

As all of you now recognise, you and your classmates are an extraordinarily heterogeneous group, but medical education is a lot like an election race. As you remember, in *Alice in Wonderland*, the Dodo set out a race course. Contestants, like medical students, could begin when and where they pleased. Following an interval, determined exclusively by the Dodo, he announced: "The race is finished." When challenged as to the winner, the Dodo was initially stumped – but soon recovered: "Everyone has won and all shall receive prizes." Like the election race contestants, you all began this medical school race from very different starting points. Although your medical school curriculum has tried to homogenise you, you all know that each of you has already run a very different educational race. In the future, the Dodo will announce that this portion of the race is over. And with your MBBS degree, you are all receiving a most prestigious prize. Now, as Winston Churchill said, "This is not the end, it is not even the beginning of the end; but it is perhaps the end of the beginning…"

As medicine pushes the therapeutic envelope, and spans the continuum from particle physics to religion, we physicians are uniquely positioned to add contextual reality to the ethical enigmas of placing new organs, new cells and new genes into our patients. We must remain involved in this dialogue.

Just how much of Uncle Andy's organs, cells, and genes can we clone, transfect and replace before Uncle Andy ceases to be Uncle Andy? In your professional lives, you will confront questions and realities that were not even blips on your medical faculty's radar screen.

Dr. Samuel Schecter

The questions and challenges you encounter will abound resplendent in glorious technicolour. Rudyard Kipling used animals to illustrate human messages. In *Just So Stories*, he notes: "In the beginning of time…the ox and the dog and the horse and the camel were each recruited to serve man. The ox, the dog and the horse willingly complied. When, asked to pull a plow however, the camel said: 'Humph'." So, as penance, the camel was given one. Kipling wrote:

> *"The camel's hump is an ugly lump, which well you may see at the zoo, but uglier yet is the lump we get for having too little to do."*

With your MBBS degree you can always be constructively busy – you will never be bored or lonely. And, we are fortunate.

Where do new clinical treatments come from? Translating knowledge into practice

Prof. Ian Frazer
Professor/CEO and Research Director
Translational Research Institute
MBChB, MD, FAA, FRCPA, FRCP(Ed), FTSE, FRS

Professor Ian Frazer is currently director of the Diamantina Institute for Cancer, Immunology and Metabolic Medicine at the University of Queensland. Professor Frazer studied medicine at Edinburgh University and trained as a renal physician and clinical immunologist. He received a BSc(Med) in 1974 and an MB ChB in 1977. He is most famous for his continued work with HPV, in particular HPV and cervical cancer. The work of Frazer with his colleague, the late molecular virologist Dr Jian Zhou, has led to the development of a vaccine which prevents infection with HPV and cervical cancer. Professor Frazer was Australian of the Year, 2006. He is also a Fellow of the Australian Academy of Science, was recently elected as a Fellow of the esteemed Royal Society of London. Professor Frazer teaches immunology to undergraduate and graduate students of the University of Queensland.

According to the Australian Institute of Health and Welfare, we gained over 25 years of extra life expectancy during the 20th century. These extra years have resulted largely from development of public health measures, vaccines and antibiotics that have reduced the impact of infectious diseases on a global basis. These interventions are the tangible result of medical research conducted by health care professionals and scientists worldwide. Over the last 100 years, there has been a slow but steady revolution in the way that medical research is conducted. What was once the province of hobby scientists, working alone in spare time and using their own funds, in lab space hidden away in hospitals and medical schools, has become a multi-million dollar business, conducted in large biomedical research institutes by professionally trained government and industry funded scientists and clinician scientists. Why has this change come about, and where is this leading?

The early drivers of medical research were the desire of the health care professions to ensure better health outcomes for their patients, and the curiosity of scientists about human physiology and pathophysiology, and these remain relevant today. However, as the technologies available for research have become more sophisticated, and the existing knowledge base more extensive, research has required more prior education, more sophisticated facilities, more collaboration, and more money. Further, the funding model for universities, the traditional trainers of researchers, has changed to one driven by quantity of throughput in addition to quality of output. In consequence, further drivers have emerged which have encouraged a more commercial and managed approach to research. These include desire of universities to maximise student numbers and research grants, government desire to see outcomes from research at affordable prices, and a growing "for profit" pharmaceutical industry hungry for the next blockbuster product, that might be expected to sell over $1billion per annum in the first years of launch. These drivers have increasingly led to focusing of research into institutes that can compete on a world playing field for resources and talent, and can afford the increasingly sophisticated infrastructure of the large scale "hypothesis free" approach to biology currently being practiced.

These drivers will likely continue to influence the conduct of medical research in the first decades of the 21st century, though some new ones have recently emerged. The supply of blockbuster drugs has largely dried up, at a time when many of the major successes of recent years are about to come off patent. This appears in part to be due to the pharmaceutical industry becoming a victim of its own success. Many of the commoner chronic diseases that require ongoing therapy already have a choice of successful drugs available: the space in the market for new ones is correspondingly limited. The future successes will likely be niche market high value products and, if current trends continue, the majority of these will be biopharmaceuticals, naturally occurring protein or peptide signalling molecules and biomimetics of these, including antibodies, and soluble receptor molecules, rather than small molecules screened from synthetic libraries for biological activity in *in vitro* assays.

Figure 1. *The Outdoor Room – a focus for collaborative activity (© Wilson Architects and Donovan Hill. Reproduced with permission).*

As we understand more of the genetic determinants of risk of chronic disease, the significance of genetically engineered animal models of these diseases for successful research will increase. These models will become a key component not only of the understanding of pathophysiology of chronic disease, but also of testing of interventions to manage, and increasingly to prevent, these diseases. A further driver of change will be the perhaps belated realisation by "big pharma" that while they are now well experienced in the manufacture and global distribution of drugs, their in-house research programs are now generally less productive and more expensive than those of universities and research institutes. Outsourcing of research from industry to academia, already widely practiced, will likely become the preferred model.

A successful future for biomedical research will likely require a partnership between government and industry to meet the costs of development of the new products required for prevention and amelioration of the common chronic diseases of an ageing population; indeed, one estimate is that more than a third of these costs are already met from the public purse, one way or another. The challenges we face with an ageing population seeking not just a long life but a long and healthy one will include dementia, mental illness, cancer, arthritis and other musculoskeletal degenerative disease, metabolic disease (type two diabetes and other consequences of obesity) and cardiovascular disease.

So what will the research institute of the near future look like, if designed to address these multiple drivers? Probably, it will resemble the new Translational Research Institute (TRI) currently being constructed in Brisbane. Institutes will likely be located in the

grounds of a major government funded teaching hospital with a strong track record in clinical research and innovation, such as the Princess Alexandra Hospital or the Mater Hospital in Brisbane, to ensure close contact with the clinical world. They will be an active part of an Academic Health sciences centre, like the newly created Diamantina Health Partners, which will bring together ten agencies responsible for health delivery on the south side of the Brisbane River, so that the institute can contribute to selection and training of key staff with teaching, research and clinical service responsibilities across several hospitals and clinics, covering the spectrum of clinical care.

Figure 2. *The North East Corner of the Translational Research Institute Facility (© Wilson Architects and Donovan Hill. Reproduced with permission).*

These "super-institutes" will bring together researchers from several different disciplines and technologies, possibly combining existing successful institutes, to share the necessary but expensive and short lived state of the art infrastructure, and to make efficient use of talent and promote scientific interactions. The Translational Research Institute, which is not so much a new building under construction as an alliance of research groups, will bring together the University of Queensland Diamantina Institute, the Mater Medical Research Institute, the Princess Alexandra Hospital Centres of Research Excellence, and the Queensland University of Technology Institute of Health and Biomedical Innovation. These partners will work in state of the art premises on two campuses, where the latest technologies for biomedical research – high speed nucleotide sequencing, proteomics, flow cytometry, animal and cell imaging, animal models of disease – will interface with clinical research facilities.

The institute of the future will likely incorporate the necessary facilities for making and testing new drugs, to facilitate their translation into clinical practice. TRI will, for example, have a facility, Biopharmaceuticals Australia, which can manufacture biopharmaceuticals to Good Manufacturing Practice standards and to a large enough scale to enable clinical trials to be conducted with locally made materials. This facility, which will be operated by a world leader in biopharmaceuticals manufacture, DSM biologics, will be available not only to the researchers from the Translational Research Institute but also more widely to the Australian Research community to facilitate conduct of clinical trials in Australia, of products arising from Australian research.

However, these technical details of what the research institute of the future will need for success do not really convey the philosophy of what I believe will be necessary for the Translational Research Institute to be successful in its ambition of sharply increasing the rate of translation of research knowledge into clinical practice. Rather, success will require bringing together people from diverse backgrounds and training, with a common passion to contribute not only to their own research programs but also to those of others, and to the training of the next generation of scientists and health care professionals.

The research focus will be on clinical problems, rather than scientific disciplines, hardly a new idea but one more often paid lip service to than put into practice, and the research standard will need to be competitive on a world stage to justify the considerable ongoing investment in the work of the institute by government and industry. These two requirements will mandate that the number and focus of the research programs undertaken will necessarily be limited: while a broad focus on cancer, metabolic medicine, infection and inflammation will be apparent, teams will be established which will focus on more specific aspects of these broad pathophysiological problems – for example, prostate and skin cancers, the metabolic syndrome associated with liver disease, autoimmune diabetes, and genetically determined inflammatory arthritic disease. Inevitably these diseases of particular interest will be the ones in which clinical expertise in the associated hospitals matches with local availability of realistic animal models of these diseases, and strong researcher interest in their underlying pathophysiology. These characteristics are the most likely to ensure that new insights from the research program will more easily cross the "valley of death" from the research bench to the clinic, leading eventually to new treatments.

The major driver of research innovation has been, and will continue to be, interactions between researchers across boundaries – interactions between scientific disciplines (mathematics, engineering, chemistry, biology); those that cross technologies (protein analysis, animal modelling) and those that cross the age boundaries (students with risky new ideas interacting with researchers who are more experienced but more conservative). The Translational Research Institute has been designed to encourage these interactions – meeting places abound, and traditional boundaries between craft disciplines will be discouraged in the layout of the facilities, and in the planning of meetings and other professional interactions.

As always, the most useful meetings will be casual conversations over coffee, and these will also be catered to. One interaction that TRI is particularly designed to encourage is to bring together the clinicians that trial new treatments with the product engineers that will produce them and the scientists that design them – an early reality check on the feasibility of a particular approach to solving a clinical problem will be the goal. Another interaction to be encouraged will be between the next generation of scientists and the current generation – SPARQ(Ed), a joint initiative of the Institute and the Queensland Government Department of Education, is a program that brings young scientists from school years 10-12 into working labs in the Institute where, mentored by active researchers, they will conduct research as part of the program of their mentors, and in the company of their school science teachers. This exposure is designed to encourage these up and

Figure 3. *Construction of the Translational Research Institute Facility.*

coming scientists to realise that their contribution to knowledge will be valuable at all stages of their careers. A further significant interaction to be encouraged across boundaries is geographical. Research students within the institute already come from every continent of the world (except Antarctica) and each brings a different perspective on the value of particular research objectives for their country, and a different approach to the appropriate methods for developing new knowledge in research.

Creation of the Translational Research Institute is, like the conduct of all medical research, an experiment. As with all experiments, there is risk, and uncertainty of outcome, but the potential benefits are considerable, and strategies are in place to mitigate the risks, which seem small in comparison with the risks of continuing to run clinically focused research as a small scale activity when the rest of the world is moving towards a different scale of activity. I was delighted to be offered the opportunity to be the first CEO and research director of the TRI, but would be the first to acknowledge that while my position comes with the responsibility of making the experiment a successful one, the major determinants of success will be the commitment of the partner institutions, and the scientists and clinicians who drive the research. The institute will succeed to the extent that they make TRI, when it opens in 2012, a world leading research institute and a model of how partnerships between government, industry and the research community can ensure a continued healthy future for the people of Australia and elsewhere. I hope that many of those of you reading this article will become a part of that success story!

Markets and medicine: Financing the Australian healthcare system

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Introduction

In early 2010 the Commission on the Education of Health Professionals for the 21st Century (the Commission) convened to outline a strategy for advancing healthcare towards a system that provides "universal coverage of the high quality comprehensive services that are essential to advance opportunity for health equity within and between countries." [1] The strategy focuses on the education of health professionals to empower their capacity as agents of social transformation. [1] This paper endeavours to encourage medical students to think critically and ethically about the consequences of different modes of health finance on the equity of the Australian healthcare system. In doing so, it contributes to this project of health professionalism in the 21st century.

Health finance may seem of little relevance to aspiring or practicing health professionals. However, it is an important determinant of how and to whom medical services are delivered and a critical aspect of Australia's response to the increasing resource demands of the healthcare system. Rising costs are attributable to a variety of trends including innovative but expensive technology, an ageing population, and increasing prevalence of lifestyle associated disease. Policy makers continue to debate the most effective funding methods to achieve effective use of resources, quality services and equity within the healthcare system.

A central issue continues to be the appropriate financial contribution of the private and public sector. Scandinavian countries and Japan rely predominantly on public spending, which accounts for 80.8-84.7% of total spending on health. Others, most notably the United States, have opted for more extensive private contribution, where public spending accounts for 46.0% of total spending (all data from 2008). [2] Australia is somewhere in between, relying on 69.7% of total spending from public funds with the private contribution making up the balance. More than 25% of total private spending is through private health insurance funds. Other private sources, mainly out-of-pocket payments made by individuals, contribute the remainder (data from the 2008-2009 financial year). [3]

The middle road approach has not excused Australia from the private/public healthcare debate. In recent years the debate has focused on the pro-private policies introduced by the Howard government in the late 1990s that reversed the decline in the number of people with private health insurance. [4-6] At the time of writing, the 2011 Federal budget, which includes substantial private/public health finance reforms, is being actively debated in Parliament and the press. [7]

The purpose of this paper is to encourage a greater understanding of the role of private healthcare and its impact on the public system through examination of two important reforms of the late 1990s: the 30% rebate; and Lifetime Health Cover. These are evaluated in terms of influence over uptake of private health insurance (PHI), government health spending and equity. This is followed by an evaluation of the effects of post-reform uptake of PHI on the healthcare system. This highlights the limits of PHI membership to reduce public spending and to relieve pressure on public hospitals. It also exposes PHI and pro-PHI policies as a source of inequity within the Australian healthcare system. Finally, the implications for medical students of the analysis are highlighted. The Commission has proposed a central role for health professionals in achieving equitable and effective healthcare systems. Thus, this paper responds to these emerging aspects of medical practice and challenges students to engage in a new kind of health professionalism.

To change the direction of the Australian healthcare system, it is helpful to know where it came from. With that in mind we begin with a brief history.

History of the Australian healthcare system

Healthcare in Australia is provided through interdependent public and private sectors that provide both equivalent and complementary services. This organisational structure is contingent on the health policies introduced in Australia since the 1950s.

Government regulation of PHI in Australia began in 1953 under the National Health Act, which strove towards universal coverage through subsidy, tax deductions and regulation of PHI. Regulation required insurers to (i) accept all applicants, regardless of their personal characteristics such as age, gender or health status; and (ii) offer community-rated premiums that did not reflect the person's risk status. In July 1975, the Whitlam-led Labour government attempted to achieve universal coverage through the introduction of Medibank. Under Medibank, doctors could opt to bill government instead of charging patients. It also provided free hospital care through state run public hospitals. [8] However, the central features of Medibank, including universal coverage, were dismantled over the following five years by the newly elected Liberal-National coalition government. In 1984, the then Labour government introduced Medicare as the national universal health insurance program; a function it continues to perform today. [8]

Medicare provides cover for primary health care, ambulatory services and inpatient care in public hospitals. It is funded through federal tax revenue and 1.5% levy on taxable income. [8,9] Private healthcare and insurance continues to exist in parallel and provides complimentary ancillary services not covered by Medicare, such as dental, physiotherapy and some equivalent inpatient services also covered by Medicare. Private patients enjoy certain benefits over Medicare including choice of consultant, shorter waiting lists and private accommodation in private hospitals. [10] Government regulation of PHI continues to reflect the mandates of the 1953 Act.

The precedent of PHI in Australia prior to Medicare and influence of

vested interest groups ensured that it remained an integral component of the national healthcare system. [8,11] However, in the years following the introduction of Medicare and the large premium increases of the late 1980s and early 1990s [9] PHI membership steadily declined (see Figure 1) and Medicare replaced the private health insurance industry as the largest funder of healthcare in Australia.

In response, an influential lobby composed of private sector interest groups, including private hospitals, insurance funds, and State governments, emerged. They argued that declining membership threatened the viability of the private sector and that previously privately insured patients would overwhelm public hospitals. [12] However, data from the late 1990s indicates that public hospital activity (measured in patient days per capita) had decreased compared to a marginal increase in private hospital activity. [8,13] Nevertheless, governments of the 1990s accepted the threat as legitimate and responded with a variety of reforms designed to increase PHI membership and enhance industry sustainability. Two reforms introduced by the Howard led Liberal-National coalition government coincided with a substantial uptake of PHI beginning in March 2000 (Figure 1) and are of particular interest. [14]

1. A 30% rebate on PHI premium payments for both hospital and ancillary cover introduced in December, 1998. This was designed to promote PHI membership by increasing affordability.
2. The lifetime health cover was introduced July 1, 2000. This enabled insurers to increase premiums 2% p.a. for anyone taking out health insurance after the age of 30, to a maximum of 40%. It was designed to encourage a younger membership and keep individuals enrolled; reducing so called 'hit-and-run' membership.

Considering the shift in PHI membership and the considerable public spending associated with the 30% rebate it is helpful to examine the impact of these policies in greater detail before considering the relative benefits of increased PHI membership.

Costs and effects of pro-PHI policies on uptake of PHI

Figure 1 demonstrates increased uptake of PHI membership following the introduction of the 30% rebate and lifetime health cover reforms. However, closer analysis reveals that the introduction of a lifetime health cover, and not the 30% rebate, should be credited for the increased uptake. Several authors draw attention to timing of each intervention. [14,16-19] Figure 1 shows the substantial increase in membership appears to be much more closely associated with the lifetime health cover deadline in July 2000 than the 30% rebate. These initial observations were corroborated at the time by survey data that evaluated health insurance purchasing behaviour and intentions. These data predicted only a small increase in PHI membership in response to the 30% rebate. [20] More recently, empirical estimates using econometric modelling confirmed that the rebate was unlikely to induce significant uptake of PHI. [21]

Beyond questions of efficacy, several other concerns are worth mentioning, including the cost and equity of the 30% rebate. In 2008/09 annual government spending on the PHI rebate reached $3.6 billion. [3] This cost increases each year in proportion to the annual increases in insurance premiums. [22] Considering the substantial and increasing annual spending the government should expect to save money through reduced use of public hospitals. Assume temporarily that the introduction of the 30% rebate was effective, overlooking the evidence to the contrary presented above. Increased PHI membership should shift patients and costs to the private sector and reduce pressure on the public system. However, in the years following its introduction researchers estimated that no more than 16.5-20% of the annual cost of the rebate was recovered through such a shift, a poor return on investment. [14,23]

Equity is also a legitimate concern. Figure 2 demonstrates that wealthy Australians are more likely to purchase PHI than poorer Australians. [24] This income gradient is problematic if equity is to be attained across the health system. All privately insured Australians are eligible for the 30% rebate regardless of income status. Consequently, the rebate disproportionately benefits wealthy Australians. [10,14,17] Furthermore, PHI covers a variety of ancillary services. This means that the 30% rebate effectively subsidises services not covered by Medicare, including dental, optical, physiotherapy, and chiropractic services. [14,17] Since wealthier Australians are more likely to hold PHI they effectively receive subsidisation of these services. Poorer Australians,

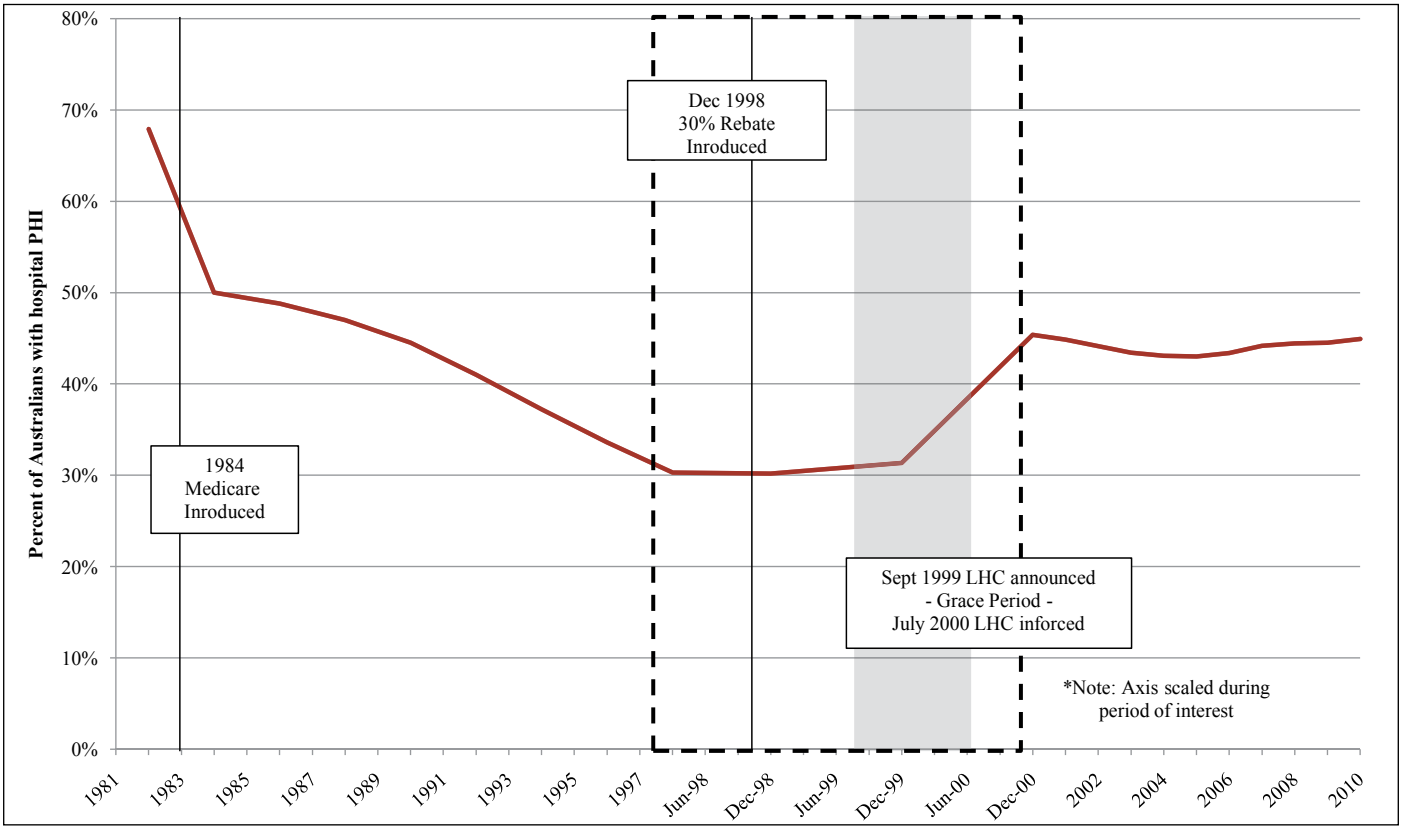

Figure 1. *The percentage of Australians with hospital private health insurance over the past 25 years. Adapted from [14,15].*

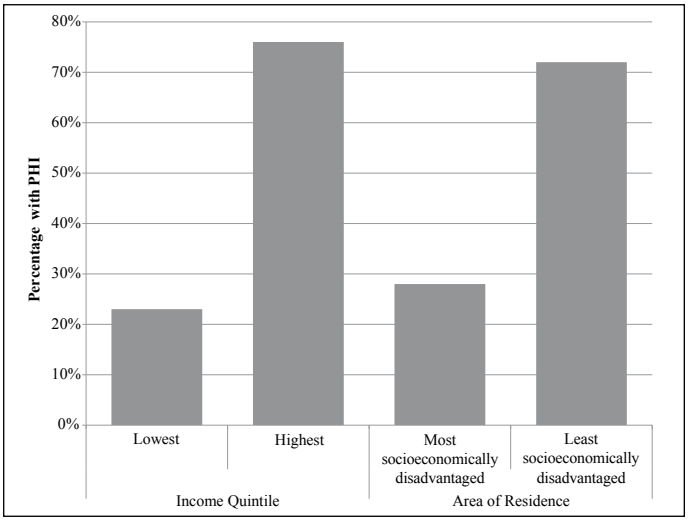

Figure 2. *Comparative percentage of Australians with private health insurance depending on income quintile and area of residence. Adapted from [24].*

unable to afford PHI, are left paying out-of-pocket or going without.

Through the 30% rebate, the government spends several billion dollars a year to sustain a sector that by its very nature compromises the equity of the Australian healthcare system. These resources could be better allocated to improve the public option available to all citizens. [25] Nevertheless it was included in the platform of reforms that caused considerable uptake of PHI.

Effect of increased PHI membership on public healthcare

Prior to the introduction of the main reforms discussed above, the 1997 Industry Commission report identified a variety of objectives met by the private Australian healthcare sector, [26] including:

1. Encouraging private funding to relieve pressure on the public purse; and
2. Relieving pressure on the public system.

The effects of increased PHI membership following the reforms can be used to evaluate the extent to which the private sector accomplishes these objectives.

Government health spending

The effect of increased PHI membership on government spending can be evaluated in terms of relative contribution of the federal government and health insurance funds to total health spending. Table 1 demonstrates that the proportional contribution of total health spending made by the government remained relatively constant during the period of reform. Furthermore, the increased uptake of PHI, although possibly associated with slowing the decline, has not increased the proportion of total spending contributed by health insurance funds. [14]

The absence of a strong relationship between increased PHI membership and increased contribution to overall health spending made by health insurance funds contradicts policy designed to increase PHI membership. This further supports the previous conclusion that the substantial spending on the 30% rebate should be redirected to the public sector to enhance the equity of the healthcare system.

Pressure on the public system

The second objective suggests that if more people are utilising private services, there will be less pressure on the public system, leading to reduced waiting periods for elective consultations and procedures. However, studies have failed to detect any change in wait times for these services following the uptake in PHI. [28,29] Several explanations have been proposed.

First, holders of PHI are still entitled to public services and may use each sector strategically to minimise cost and wait times. [30] This may be exacerbated by the fact that there has been a concurrent increase in uptake of PHI with large co-payments that encourage use of the public system for more services. [14] Indeed, some PHI members may not utilise private services at all and instead enrol in PHI simply to avoid the tax surcharge on high income earners. [14]

Second, consistent with the intention of the lifetime health cover reform, PHI uptake was greatest among young individuals. [17]

Table 1. *Relative contributions (in percentile) to total health spending over the past fifteen years. Some rows may not add to 100% due to rounding. Data ranging from 1998/99 - 2008/09 sourced from the Australian Institute for Health and Wellbeing report Health Expenditure Australia 2008-2009. [3] Data ranging from 1992/93 - 1997/98 sourced from the Australian Institute for Health and Wellbeing report Health Expenditure Australia 2002-2003. [27]*

	Government			Non-Government			
Year	Federal Government	State/territory and local	Total	Health Insurance funds	Individuals	Other	Total
1992–93	43.6	23.4	66.9	11.4	16.8	4.9	33.1
1993–94	45.1	21.3	66.4	11.0	16.9	5.6	33.6
1994–95	44.8	21.6	66.3	10.7	17.1	5.9	33.7
1995–96	45.2	22.0	67.2	10.5	16.0	6.3	32.8
1996–97	43.7	22.9	66.7	10.4	16.7	6.3	33.3
1997–98	44.4	23.8	68.2	8.8	16.7	6.3	31.8
1998–99	43.3	23.7	67.0	8.0	17.3	7.8	33.0
1999–00	44.3	24.9	69.2	6.9	16.7	7.3	30.8
2000–01	44.4	23.3	67.7	7.1	18.0	7.2	32.3
2001–02	44.0	23.2	67.2	8.0	17.5	7.2	32.8
2002–03	43.6	24.4	68.0	8.0	16.7	7.3	32.0
2003–04	43.6	23.6	67.2	8.1	17.5	7.3	32.8
2004–05	43.8	24.0	67.7	7.7	17.4	7.1	32.3
2005–06	42.8	25.3	68.0	7.6	17.4	6.9	32.0
2006–07	42.0	25.8	67.8	7.6	17.4	7.2	32.2
2007–08	43.2	25.5	68.7	7.6	16.8	6.9	31.3
2008–09	43.2	26.5	69.7	7.8	16.8	5.7	30.3

Relatively speaking, young individuals are not major consumers of healthcare services in either system and are likely to make fewer claims on their policies. This shift favours industry sustainability but is unlikely to take any pressure off the public system. [14]

Finally, supply of healthcare resources, especially human resources, is limited and stable in the short term. Every patient treated privately tends to consume human resources that could otherwise be utilised in the public system. Indeed, evidence suggests that for any specialty, as the proportion of surgeries performed privately increases so does the wait list in the public sector. [31]

Implications for the health system and health professionals

The failure of the private sector to control public spending and pressure on the public system despite substantial uptake of PHI highlights the complexity of the relationship between parallel private and public sectors. Hurley *et al.* [10] emphasise that sustainability of the private sector depends on the quality of healthcare it offers. Crucially, when a public and private sector operate in parallel, the public sector must be inferior to the private, or there will be no incentive for individuals to pay for private services that are offered free of charge in the public system. [10] Considering wealthy Australians are more likely to hold PHI, this implies a two-tiered model of healthcare is unavoidable and presents a clear threat to the equity of the Australian healthcare system. Indeed, wealthy Australians tend to have access to better healthcare and have better health outcomes. [32,33] These realities constitute a central challenge to the role of the private sector within the Australian healthcare system.

Despite these persisting inequities, change is possible but requires leadership and commitment. The Commission argues that health professionals are privileged because of the time and effort spent training, and the investment by families, society and public financing. We therefore have an obligation to act on behalf of our investors, educate ourselves, think critically and ethically, and become advocates for effective and equitable health systems. [1]

The present aim is to challenge students to critically examine the financial policies and mechanisms of the Australian healthcare system with specific attention to the implications for equity. In doing so, this paper highlights emerging aspects of medical practice and contributes to the project outlined by the Commission to educate health professionals to "mobilise knowledge, and to engage in critical reasoning and ethical conduct." [1] Such an education empowers us to become agents of change within the health system who strive for a more equitable future. [1]

Conclusion

In an effort to challenge medical students to engage in a new health professionalism outlined by the Commission on the Education of Health Professionals for the 21st Century, this paper provides a critical evaluation of the health finance system in Australia. This evaluation centred on the effects of two pro-PHI reform platforms introduced in the late 1990s. Despite contributing to substantial uptake of PHI, these reforms failed to relieve pressure on the public system or control public costs. Through evaluation of these reforms a critical analysis of private health finance and service delivery has also emerged. The analysis revealed the complex relationship between activity in the private sector, insurance and delivery, and the pressure felt by the public healthcare system. Moreover, the evidence presented provides a cautionary discussion about the real limits of parallel private healthcare. Most concerning are the persisting socioeconomic inequities within the Australian healthcare system. This discussion provides some insight into the complexities inherent in the public/private debate, prepares medical students for informed engagement with these issues, and in turn contributes to a new health professionalism of the 21st century.

Acknowledgements

The author would like to thank Tracey Stock, Sarah Lord and Jarrod de Jong for their helpful and insightful comments on earlier drafts of this manuscript.

Conflict of interest

None declared.

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Is mandatory pre-procedure ultrasound viewing before termination of pregnancy ethical?

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Maryam is a final year medical student at the University of Sydney. She received the Cedric Swanton Memorial Prize for Psychiatry in 2010 and has an interest in mental health and medical ethics.

Sally is a pregnant nineteen year old woman at eight weeks gestation. Sally is currently serving time in gaol and has arrived at the hospital gynaecology clinic with several members of Justice Health.

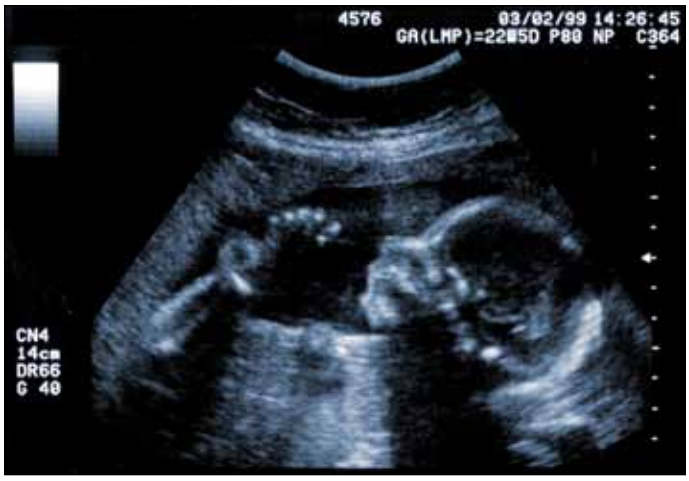
Sally is informed that the hospital can offer surgical termination of pregnancy and she is advised about the possible complications and risks of the procedure. Upon hearing these, Sally becomes tearful. The doctor advises Sally that she should not terminate the pregnancy if she has any uncertainties. Sally explains that she is concerned about the risks of the procedure, but still wants to go ahead with the termination.

As part of her initial assessment, the doctor performs an ultrasound. The consultant points out the fetal poles and heartbeat stating, "Here is the baby's heart beating." Upon hearing this, Sally begins crying and becomes withdrawn, not responding to any questions. The doctor concludes that Sally should be given more time to contemplate whether she wants to terminate this pregnancy and does not book her in for the procedure.

The above clinical example raises a number of ethical issues in regards to abortion. Can the woman make an informed choice without coercion when she is shown the ultrasound in this manner? Is the autonomy of the patient compromised when she is forced to listen or view information that is not necessary to her medical care? Is it in the patient's best interest to show her the ultrasound without first asking her preference? In this article I will focus on the medical ethical values of autonomy, informed consent and beneficence in regards to the use of pre-procedure ultrasound for abortion.

One in three Australian women will have an abortion during their lives, and most Australians do not support increasing restrictions on the availability of abortions. [1] Reasons for abortion are multi-factorial and relate to not wanting a child at the present time, maternal health, partner reasons as well as financial and housing limitations. [2] The majority of women who seek abortion were using contraception at the time they fell pregnant, highlighting the need for increased contraceptive education and options. [1] Abortion laws in New South Wales are relatively liberal, allowed on the grounds of preventing mental or physical harm to the mother, and in practice are freely available without restriction in the first trimester of pregnancy. [1] The abortion rate has changed little in Australia over the past twenty years and was 19.7 per 1,000 women in 2003, comparable to that in Sweden, New Zealand and the United States. Interestingly, countries with more liberal abortion laws such as Germany and Switzerland actually have lower abortion rates than Australia. [1]

The current Royal College of Obstetricians and Gynaecologists guidelines recommend ultrasound assessment before termination of pregnancy in order to confirm the gestational age, intrauterine location and viability of the fetus. [3] In New South Wales (NSW), the woman is not legally required to view the ultrasound during assessment, but changes are currently being proposed in parliament that would force women to view an ultrasound of their fetus before the procedure. [4] Several states in the United States, such as Oklahoma, have already established a similar law that requires every woman seeking an abortion, even if she is a victim of rape or incest, to view an image of the fetus prior to the procedure and listen to a detailed description of what can be seen. [5] Supporters claim that viewing the ultrasound is empowering, enabling the woman to make a fully informed decision.



However, it can also be argued that such government imposed restrictions are an invasion of patient autonomy, limiting a woman's access to abortions by placing limitations on how her decision can be made.

In the above clinical example, the health care team had a number of different options in managing this patient. They could have asked Sally whether or not she wished to view the ultrasound. Additionally, the doctor could have used less emotive language when describing the ultrasound or not described it at all in the presence of the patient. Since there is no current legislation in NSW requiring the woman to view the ultrasound, all of these options would have been legally sound. However, ethical issues of autonomy, informed consent and beneficence can be argued for each case.

Does the woman need to be shown the ultrasound in order to make an informed decision? Informed consent is defined as consent that is freely given without coercion from external influences such as hospital staff and family. It also requires that the patient is aware of the diagnosis, recommended treatment and significant risks associated with the procedure. [6] The woman is already well aware that she is pregnant, and therefore would satisfy the requirement that she is aware of the diagnosis without requiring to view the ultrasound. It seems unnecessary that she should require more detailed information about her pregnancy in order to make an informed choice. It can be argued that forcing the woman to view the ultrasound is a form of coercion, thereby making the patient's consent invalid. This is particularly true when the procedure is mandated by government legislation, as is the case with compulsory pre-procedure ultrasound viewing in Oklahoma, where it is unclear whether policy-makers' intentions are in the best interests of patient or in furthering political or religious agendas. Patient autonomy, the right of the patient to make informed decisions about personal matters, is clearly broached when legislation is introduced that places extraneous limitations on a woman's decision making process. Furthermore, the beneficence of such actions is questionable; whose interests are they really serving?

A Swedish study has shown that the majority of women describe feelings of relief in the short term after an abortion, a finding replicated by studies in other countries, [7,8] and two-thirds do not experience emotional distress in the long term. [9] Those who described feeling

no emotional distress had not experienced conflict of conscience or pressure during the decision making process. Those with the highest levels of post-abortion distress were more likely to have experienced coercion during the decision making process. [9] The core medical value of beneficence requires medical practitioners to take actions that serve in the best interests of their patient. If the best psychological outcome of abortion is achieved by limiting coercion, a woman's choice should be free from restrictions and she should be able to choose whether or not she wishes to view the ultrasound as part of her decision making process. What benefit does the patient gain by increasing distress related to the procedure by not providing her with this choice?

There are few studies available that have examined women's perceptions about pre-procedure ultrasound before abortion. A recent Canadian study analysed the experiences of 350 women attending an abortion clinic who were given a choice of viewing the ultrasound before abortion. Seventy three percent of women chose to view the ultrasound and of these, 86% found it to be a positive experience. None of the women in this study changed their mind about having an abortion after viewing the ultrasound. [10] A French study found the opposite to be true, with most women requesting not to see the ultrasound. [11] This highlights that all or nothing measures are not the best option, as women's preference for ultrasound is not always predictable. The current guidelines state that "When ultrasound scanning is undertaken, it should be in a setting and manner sensitive to the woman's situation," supporting the notion that a woman's wishes should be taken into account when the ultrasound is performed. [3]

Sally is clearly in a complex and difficult life situation, facing many social and psychological issues relating to her incarceration and unwanted pregnancy. Unfortunately, Sally was not given a choice in viewing the ultrasound during assessment, and became distressed upon seeing the fetus. This situation can be generalised to all women seeking abortion in NSW, where there is no legislation to force a woman to view the ultrasound, but it is not compulsory for women to be asked their preference on the matter either. From the viewpoint of medical ethics, the patient seeking an abortion should have the right to autonomy and to provide informed consent for the procedure. In light of the evidence, I believe that informed consent can only be valid if the woman has been given a choice before the ultrasound is shown. Some women may prefer to view the ultrasound as part of their decision making process while others do not want the added distress. If she is forced to view the ultrasound, this can be interpreted as a form of coercion, whether intentional or not. The beneficence of this act is also questionable, as it is certainly not in the best interests of the woman to place restrictions on how she can make her decision.

Clinical decisions are sound when based on current, good quality evidence and more research needs to be performed on the psychological impact of pre-procedure ultrasound before one can definitively argue whether viewing the ultrasound is beneficial for the patient. Based on current evidence, the option that best promotes patient autonomy and beneficence appears to be asking the woman before performing the ultrasound whether or not she would like to view it. Not viewing the ultrasound still fulfils the conditions of informed consent, as described above. It is not the viewing of the ultrasound which is unethical but the fact that the woman has no say in the matter. As such, policy directives in the future should be clearer about how ultrasound is used during the assessment of termination of pregnancy and aim to promote beneficence while respecting patient autonomy.

Conflict of interest

None declared.

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Self-taught surgery using simulation technology

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Behnoosh graduated from UNSW in 2010 and is currently working as an Intern at Hornsby Hospital, Sydney. Her elective experience fuelled her passion for surgery, particularly fostering an interest in laparoscopic upper gastrointestinal surgery. Behnoosh hopes to specialise in this area but also has interests outside of medicine, which she hopes to continue during her busy work years. She dabbles in the fine arts, languages and soccer.

During my elective term in early 2010 at the Royal Free Hospital, London, I was presented with a fantastic opportunity: to learn how to perform a laparoscopic gastric bypass procedure. The challenge was for myself, a medical student and complete novice in laparoscopic surgery, to use the hospital's state-of-the-art screen-based simulation technology to become proficient in a specific operation within six weeks in this rapidly advancing area of surgery.

My training was to be undertaken using the Simbionix LAP Mentor (Simbionix, Cleveland, Ohio, USA): an advanced piece of technology made up of a computer with simulation software and accompanying hardware, consisting of ports and instruments. The difference between this and a video game is the presence of haptic feedback; when you hit something or pull it, you feel the corresponding tension, making it a highly realistic representation of surgery.

The training schedule consisted of successive steps to gradually build the skills and knowledge required for the real operation. I was to dedicate time every day for training on the simulator, in addition to background research. I was supervised by the head of the simulation centre Dr. Pasquale Berlingieri, a laparoscopic gynaecological surgeon, and my elective supervisor, Mr. Zak Rahman, a laparoscopic hepato-pancreatico-biliary surgeon.

The first step was to complete the "basic tasks" module on the simulator, which was aimed at training my hand-eye coordination, depth perception and an awareness of three-dimensional space on a two-dimensional screen. This was done by familiarising me with the instruments, as well as specific manoeuvres used in laparoscopic surgery, such as two-handed tasks of grasping and clipping or cutting.

The second step was to complete and achieve an accepted standard of proficiency (as measured by the simulator) in the "laparoscopic cholecystectomy" module. It consisted of three tasks that comprised almost all of the operation but with increasing complexity and difficulty levels: "exposure of cystic duct and artery," "separation of the gall-bladder from the liver pad" and "procedural task" which involves clipping and cutting the cystic duct to separate the gallbladder completely. Laparoscopic cholecystectomy is a relatively simple operation compared to a gastric bypass. It is also a procedure I had previously studied and seen many times. It would essentially serve as an introduction to imitating real operations on the simulator and to practice the application of the basic skills learnt in the previous module.

Concurrently, I studied the theory behind performing a laparoscopic gastric bypass procedure using primarily web-casts from sources such as YouTube© (YouTube, LLC) [1-3] and ORLive© (ORLive, Inc.). [4] I broke the operation down into steps that I could understand and described the most common techniques, that is, the proximal Roux-en-Y, as well as subtle variations, thereby developing my own preferences for techniques – just like a real surgeon. I familiarised myself with the laparoscopic instruments used, as well as their advantages and disadvantages, thereby developing my own preferences for tools – just like a real surgeon. For example, I preferred to use a linear stapler, which seemed easier to operate, as opposed to a circular stapler, and therefore the corresponding technique of performing the bypass procedure. I also observed Mr. Sufi and Mr. Rahman perform the real procedure at the Whittington Hospital to fully understand the procedure and to have my unresolved questions answered.

The third step was to commence the "laparoscopic gastric bypass" module. This involved adapting my knowledge and understanding of the procedure to the steps described in the module, which were slightly different, as well as any limitations of the simulator. This module consisted of four tasks that essentially covered the bypass procedure broken down into the four fundamental stages of the operation: creating the gastric pouch, dividing the jejunum, the jejuno-jejunostomy and the jejuno-gastrostomy.

The final step of the training schedule was to advance the simulation of the operation by simulating the environment in which the operation takes place, that is, the operating theatre. I performed the operation on the simulator with people watching me, talking and noise in the background, dressed in scrubs and wearing gloves.

I advanced on to the successive module by the end of each week, and confirmed what Dr. Berlingieri already suspected: the new generation of medical students have the ability to learn such skills quickly; not just because of our youth, but because we have grown up in an age of rapid technological advancement and therefore can adapt to new technologies quickly. I believe the aptitude for this type of problem-based learning and self-direction through the use of emerging technologies and the internet is common to all medical students today. See for yourself: my simulated operations can be seen on YouTube on the channel 'ScreenBased' (http://www.youtube.com/user/ScreenBased).

Early training of medical students in surgery using screen-based simulations presents many immediate advantages: it offers a way for the student to acquire the skills and knowledge of a particular procedure without setting foot in the operating theatres. This gives the student confidence and the aptitude to participate in the surgery and build surgical experience with minimal risk to patients. Screen-based simulations also afford the opportunity to observe and understand anatomy, complications of surgery, and limitations of the procedure. In addition, surgeons themselves can be reassured that the student is well-versed in the steps of the procedure.

But is it practical? The technology is still very new and there are still many limitations to its implementation. A single virtual reality laparoscopic surgery trainer costs around AUD$140,000. The expense of the machine, insurance, maintenance and warranties are hard to afford. Furthermore, the machines are still being fine-tuned and new programmes are constantly being developed. The current programmes

are limited in methods and materials. For example, there's no option to place 'stay-sutures' to fix the position of the bowel for jejuno-jejunostomy.

There are still some technical 'glitches' in the hardware and the software, such as pixel-errors, that need to be addressed. The program itself is quite temperamental and regularly freezes. The hardware (instruments in particular) are extremely delicate and any slight mishandling can result in hundreds of dollars worth of damage.

Obviously there is no way to programme for the vast amount of patient-specific variations encountered in real operations. It therefore stands to reason that the technology, despite its advanced nature, cannot properly equip a trainee to adapt to these complications, which is essential for the safety of the operation.

Nonetheless, though the knowledge and experience gained from the simulator is superficial, I believe it still provides an excellent platform from which to launch into the many years required for real surgical training. Personally, I found the most successful aspect of the simulator was not in the technical skills or knowledge gained, but the passion for surgery that it nurtured. It is feasible, therefore, to suggest that in the very near future, a programme of "self-directed learning" via the simulators can be integrated into the surgical rotations of medical students or junior doctors and even registrars in hospitals and medical schools.

Acknowledgements

Dr. Pasquale Berlingieri, Mr. Bimbi Fernando, Mr. Zak Rahman and Mr. Pratik Sufi.

Conflict of interest

None declared.

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A week in the Intensive Care Unit: A life lesson in empathy

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Empathy is the sharing of emotion with another sentient being. It comes from the Greek words *em* (meaning "to put into") and *pathos* (meaning "suffering") and is believed to be the essential humanistic foundation of effective health care. [1]

Empathy and the medical student – Practice makes perfect?

The observation of another person in a particular emotional state has been shown to activate a similar autonomic and somatic response in the observer without the activation of the entire pain matrix, not requiring conscious processing, but able to be controlled or inhibited nonetheless. [2] This effectively means that when we see someone in physical or emotional distress, we too experience at least some aspect of that suffering without it even needing to be in the forefront of our consciousness. As medical students we are constantly told to "practice" being empathetic to patients and family members. What we are really practicing is consciously processing this suffering we unknowingly share with these people in order to develop rapport with them (if not just to impress medical school examiners).

We are taught an almost automated response to this distress, including a myriad of body language and particular phrases, such as "I imagine this must be very difficult for you," to indicate to a patient that we are aware of the pain they are in. Surveys amongst critical care nurses have shown that gender, position, level of education and years of nursing experience have no significant relationship with the ability of a person to show empathy. [1] Thus it could be said that empathy is less of a skill which can be practiced until perfect, and more of a mindset that makes us as human as the people we treat.

Some argue that medical student cynicism increases through medical school which can then contribute to a decrease in empathy over time. [3] A particular study involving 650 students of the Boston Medical School used the Jefferson Scale of Physician Empathy (JSPE) to quantify the empathy of the students. [4] Alarmingly, the first year class had the highest empathy score while the fourth year class had the lowest and all JSPE scores were higher in females. [4] Students with an intention to pursue a people-oriented specialty (for example, general practice or emergency medicine) were found to have significantly higher empathy scores than those wishing to pursue a more technology-oriented specialty.

The decline in empathy over the years spent at medical school could possibly be attributed to stress, fatigue or an increase in workload while undertaking clinical placement. Students with an intention on following a patient-centred speciality may have a greater awareness of their need to validate the concerns of their patient. Students in a more technological-based specialty may have less demand on them professionally to show empathy. However, these students will still have to pass their clinical years in medical school and complete their internship, neither of which can be solely spent in their desired technological-based field. This is cause for great concern as while these students seem to have less empathy, they will still have to deal with emergency and critical care, general medicine and surgery much like their more empathetic counterparts, all of which have their fair share of distressing circumstances and thus a need to show empathy.

Empathy and the physician – All in a day's labour

It has been noted by Hochschild in the book "The Managed Heart" that empathy is considered to be "emotional labour" in the work of a physician. [5] The way that the physician performs such labour can

be through either faking their external emotional appearance (that is, facial expression, voice and posture) to give the impression of empathy, or through acting on emotions that they physically feel at the time. [5] The main difference is through acting on emotions, a physician focuses on changing their internal emotion state by changing their perception of the situation. In faking or using rehearsed empathy, a physician is merely changing their expression rather than their perception of the patient's experience. While using the more superficial approach has its benefits when time does not permit a more involved response, it has been contended that physicians are more satisfied professionally and are more effective as healers when they engage in a deeper level of empathetic processing. [5] Efficiency as a healer does not mean saving every patient. For those in particularly grave circumstances where little can be done, this has more to do with making the patient as comfortable as possible while also validating the emotions experienced by those around them.

My experience with empathy – Rudy's story

I lost my dear grandfather Rudy in July 2010. After an unexpected accident at home, he was taken to hospital, where 48 hours later he lay fighting for life in the Intensive Care Unit (ICU) after complications on the operating table. I had lost track of the number of times I had been lectured on empathy by the University. It was only when the tables were turned and when I played the role of the concerned family member that I truly understood the powerful effect a genuinely empathetic doctor has.

While it felt like much longer, my family spent a week in the ICU waiting room. The poorly coordinated blue walls and carpet encompassed two very old and worn sofas on which families spent any number of anxious hours waiting for news on their loved ones. During my grandfather's stay, we befriended half a dozen other families within those blue walls, united in our efforts to do whatever we could to bring our loved ones out of the ICU. In the most sterile of environments, I witnessed the rawest of emotions. I saw the anger in the parents whose daughter had overdosed and the desperation in the wife whose husband lay critically ill from an easily preventable accident. I saw the hopelessness in the children of a father who lay debilitated by long term illness and the overwhelming joy in those very few lucky families able to move their loved ones onto the wards. However, the most universal emotion was one of disbelief – not one of the families had thought these circumstances could ever happen to them.

As the week progressed, one by one each of the families disappeared. Many were lucky enough to see their loved ones reach the wards. Many

were also faced with the traumatic realisation that they would be going home without them. On the fifth day of our stay, we were told that the ventilator had to be removed, and that it was up to Rudy to fight what seemed like the impossible fight. No words can truly describe the pain, anguish and sheer terror experienced by a patient's family when their loved one has to fend for themselves. It was here that the nursing staff truly excelled. When various doctors told us (some more harshly than others) to be more realistic and less optimistic, the nursing staff took a different approach. While the circumstances were grim, these fine men and women did a remarkable thing – they put themselves in our shoes. They realised that there was little we could do as a family, but instead promised that as a healthcare team they would do everything in their power to help us and Rudy get through this. This meant the absolute world to my family, especially my grandmother, who feels forever indebted to these nurses for providing her with the one thing she really needed in the situation – empathy.

Around midnight two days later, we were summoned to the ICU for Rudy had taken a turn for the worst. We sombrely sat together for nearly six hours, holding his hand and stroking his hair, frantically saying everything and anything that we thought he would want to hear before he passed away. While excruciatingly sad, there was an air of calm about the situation and it was not until the moment that Rudy took his last breath that I realised why. As a family member, you hold onto a tiny glimmer of hope until that final heart beat, after which nothing but utter disbelief remains. When this calm was broken by the uncontrollable sobbing of my family, it suddenly felt as if my whole world had imploded. I will forever remember this moment as one of incredible heartache, including the very startling realisation that I did not want anyone to tell me they were sorry or that I was going to be okay, but that this gut-wrenching pain was not disproportionate to the circumstances and that I was not invisible to those around me in experiencing it. We found this in the doctor on duty at the time. He offered a warm handshake or a hug to anyone who needed it. He even sat with my grandmother and cried with her, sharing her pain as the doctor himself had only recently lost his mother in similar circumstances. While no amount of empathy or tears could bring my grandfather back, the fact that someone took the time to truly appreciate my family's anguish did an insurmountable help.

My grandfather was someone who took everything as a learning experience, and I believe this to be the greatest, albeit saddest, one of my life so far. One of the very last things my grandfather said to me was that I was going to make a good doctor one day. He was an amazingly compassionate man and I can think of no better way to honour him than to strive to become the best empathetic doctor that I can be.

Acknowledgements

I would like to acknowledge the outstanding staff of the Gold Coast Hospital ICU ward for their empathy and respect for my family during our time with them.

Conflict of interest

None declared.

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Should artificial resuscitation be offered to extremely premature neonates?

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Introduction

"*'Change' is scientific, 'progress' is ethical; change is indubitable, whereas progress is a matter of controversy.*" – Bertrand Russell

Forty years ago it was generally accepted that a baby born more than two months premature could not survive. Now neonates as young as 22 weeks can be kept alive with medical intervention. This essay will explore the medical, social and legal aspects of artificial resuscitation of extremely premature neonates and argue for a change to a palliative approach towards infants born at the threshold of viability.

Background

Extremely premature newborns face a number of medical problems, affecting almost all systems of the body. These problems include extreme skin immaturity and fluid balance instability, lung immaturity and breathing problems, malnutrition and gut damage, retinopathy of prematurity, early and late onset infections and brain damage which can lead to a spectrum of long-term neurological sequelae. [1,2]

Infant survival and long-term prognosis improve with increased gestation. According to the largest collaborative clinical audit to date, survival rates of extremely premature infants vary from 1% at 22 weeks to up to 44% at 25 weeks. Before 21 weeks and six days, no published studies record that a baby survived to leave hospital. [3] The fact that almost half of the infants born at 25 weeks survive has been used to justify aggressive intervention in this age group. However, of the children who survived at 25 weeks, only 20% were living with no disability by age six and 22% had severe disabilities, including cerebral palsy. [4,5] Recent Australian data on the outcomes of extremely premature neonates paints a more promising picture, with 71% surviving to eight years and 43.9% having no disability at age eight. The rate of severe disability at age eight was 8.6%. [6] However, this data includes neonates up to 28 weeks and there is no sub-group analysis of survival rates of neonates born at 25 weeks, a group known to have poorer outcomes than extremely premature neonates born at 26 or 27 weeks. [7]

Care for extremely premature newborns is extraordinarily expensive. In 2003, premature newborns accounted for approximately US$18.1 billion in health care costs in the United States (US), or half of total hospital charges for newborn care. [1] This figure does not account for ongoing costs for the health system and the physical, psychological and emotional impact of raising a child with a disability.

Although there has been much media attention regarding premature newborns over the years, the issue of their care has been given scant attention in the courts in Australia. Legal precedents originate in the United Kingdom, with the Court of Appeal ruling on the issue in 1993. Here they stated that while doctors and parent/s may not undertake actions where the purpose is to end life, they may, in appropriate circumstances, use drugs to relieve pain and distress, even though their use may advance the time of death. [8]

In the US, no court has ever ordered the withholding or withdrawal of life-prolonging interventions over a family's objections. [9] In 2003, a US court came to a controversial legal decision, permitting physicians to disregard parental preference for palliative care and unilaterally initiate resuscitation when faced with the birth of an extremely premature baby. [10]

In Australia, practice is predominantly guided by local and international guidelines rather than legal decisions.

The ethical dilemma

As stated, in the last two decades, improved survival rates of extremely premature newborns have resulted in life-saving support being offered to infants of borderline viability. The problem with increased survival rates of extremely premature newborns is that there is a corresponding increase in short- and long-term medical and psychological problems resulting from such a premature birth. This raises the pertinent question of whether neonatologists should be initiating care for these infants in the first place.

Possible choices

There are a number of frameworks which can help inform the parlous decision of whether or not to initiate treatment. The two prevailing frameworks are:

1. *The Best Interests Standard: Acting in the "best interests of the patient." Particularly attempting to determine:*
   - degree of suffering involved in the care;
   - futility of further intervention; and
   - likelihood of survival free of serious disability and practical consequences. [11]

The Best Interests Standard is a moral and legal standard for directing the decision-making process when individuals lack decision-making capacity. The interests and welfare of the patient take priority over all other parties. In this particular situation, the interests of the neonate are inextricably linked to that of the parents and therefore their interests must also be taken into account. In Australia, if the Best Interests Standard is maintained, the fiduciary duty of the clinician has been met. In the Netherlands the best interests principle permits active euthanasia of a newborn, as outlined in the Groningen Protocol. [12]

When discussing medical practice, the 19th century physician William Osler wrote: "Errors of judgement must occur in an art which consists largely of balancing probabilities." [8] The problem with the likelihood of survival free of serious disability is that this likelihood is determined by average survival rates. This is inevitably imprecise in predicting individual survival, or individual disability and suffering

for that matter. Medical practitioners cannot make a completely accurate prediction of the outcome for an individual infant. However, availability of epidemiological data and increasingly reliable diagnostic and prognostic tools have substantially reduced error in diagnosis and prognosis. We are in a better position to determine futility of treatment for premature newborns than ever before.

2. "Baby Doe Rules"

The "Baby Doe Rules" are formally known as the Child Abuse Amendments to Public Law 98-457. These US regulations prohibit anyone from withholding or withdrawing food, water, medications or other treatments appropriate to maintain survival, allowing only three exceptions for withholding life-supporting treatments:

- "The infant is chronically and irreversibly comatose;
- The provision of such treatment would merely prolong dying, not be effective in ameliorating or correcting all of the infant's life-threatening conditions or otherwise be futile in terms of the survival of the infant; or
- The provision of such treatment would be virtually futile in terms of the survival of the infant and the treatment itself under such circumstances would be inhumane." [13]

These regulations are overly prescriptive and have resulted in declined autonomy of parents and medical staff in the US. The option to make individualised and compassionate decisions, such as provision of adequate pain relief and withdrawal of some medications, hydration and nutrition in situations of futility, must be retained. On these grounds, the Baby Doe rules should be rejected.

To return to option one, the Best Interests Standard, it is apparent we have two options – decision making at birth and decision making after the infant has been resuscitated and stabilised.

Decision-making at birth is marred by uncertainty as fetal prognosis is rarely clear-cut at this point. The initiation of resuscitation leads to admission to the neonatal intensive care unit (ICU), which may set off a cascade of expensive and uncomfortable or painful procedures and raise parental expectations about survival. [14] Others contend that denying intensive care a priori, based solely on the age of gestation or birth weight, is contrary to the principle of equity. [15]

Decision-making after initial resuscitation, that is the decision to continue or withdraw treatment, may be viewed as a more justifiable alternative as it allows a better assessment of diagnosis and prognosis. It may further enhance parent and doctor autonomy by conferring a sense of control over the situation. However, many clinicians find it relatively easier to make a decision not to commence treatment rather than to cease it. There may also be reluctance from parents to "turn off life support" for their newborn too, believing they are actively giving up on their child.

The interested parties

The Patient

A newborn infant is unable to express an opinion, and its interests are represented by their parents/carers and the medical staff involved in its care. [8] The best interests of a neonate are thus entirely based on the perception of others, namely parent/s or medical staff.

At present time, it is impossible to determine what values and beliefs a neonate has, if any at all. A number of influential philosophers, including Peter Singer, argue that newborns lack consciousness and thus have no interests or independent rights. [9] Although unable to articulate their views, one cannot deny that newborns experience pain and discomfort. Maximising good and minimising harm must be paramount in treatment of the newborn.

The Carers

The neonatologist is often the default decision-maker. They hold a privileged position having knowledge of diagnosis, likely prognosis and outcome of the patient. Usually, they will give their assessment of the situation to the parent/s and ask for their consent in the management. In areas of uncertainty, the so-called "grey zone," parents have an increased role in the decision-making process. [16,17] Too much emphasis on parent choice may result in undue stress and burden of responsibility in an already stressful situation. The onus must not rest solely with the parents to decide on commencing or ceasing intervention.

Up to two-thirds of extremely premature births have complications which bring them to the attention of the obstetrician days or weeks before delivery. [11] This allows pre-delivery counselling. This counselling must be accompanied by support and engagement in the decision-making process, preferably by both an obstetrician and neonatologist. Decisions made by parents before birth are not necessarily absolute and binding.

The one principle which underlies guidelines in all advanced countries is primum non nocere. This can justify the withdrawal of life sustaining treatment if the continued treatment has a perceived worse outcome than death. There are a number of factors which affect a neonatologist's decision to withdraw treatment including hospital policies in certain countries, individual factors such as gender, age and length of professional experience, religiousness and personal attitude towards sanctity versus quality of life. [14]

The Nuffield Council on Bioethics has made recommendations about resuscitation and continuing intensive care of extremely premature infants. [11] These are shown in Table 1. The Nuffield recommendations reflect modern practice in the United Kingdom.

Table 1: *Summary of recommendations for the resuscitation at birth of babies born at borderline viability. [11]*

Gestation (completed weeks)	Standard	Exceptions
21	No resuscitation (considered as an experimental procedure)	Only as part of research protocol.
22	No resuscitation	At parents' request after prolonged and fully informed discussion of the risks, implications, and the likely outcome.
23	Could not be defined	... precedence (should be given) to parent's wishes. If left to clinicians, the clinical team should 'determine what constitutes appropriate care for that particular baby.'
24	Resuscitation	*Unless* parents and clinicians agree in the light of the baby's condition that it is not in his or her best interests.
25	Resuscitation	*Unless* severe abnormality incompatible with any significant period of survival.

In alignment with these recommendations, infants of 24 and 25 weeks are ventilated and intensive care measures implemented. The decision to withdraw assisted ventilation is made only after the infant has been given a chance of life when there has been time to assess progress and response to treatments. As mentioned above, many clinicians find it relatively easier to make a decision to not commence treatment rather than to cease it; thus withdrawal of ventilation may not be undertaken as likely as it should.

In Australia, a consensus statement exists regarding decision-making

about newborns of borderline viability. This framework considers the gestational "grey zone" to be between 23 and 25 weeks. The guidelines make recommendations in alignment with the Nuffield recommendations but essentially leave initiation of treatment to the discretion of parents and treating clinicians for newborns at the threshold of viability. [18,19] These guidelines can be interpreted on a case-by-case basis according to comprehensive postnatal assessment of the child's general health. Factors such as availability of resources, planned pregnancy, assisted conception, maternal age and illness and fetal conditions or compromise all play a part in the decision of whether to initiate resuscitation.

Australian and international surveys of obstetricians and neonatologists about their management decisions in extremely premature infants have shown significant variation in the use of intensive care in the extremely premature. [20,21] Lorenz *et al.* [22] compared management strategies in the US to those in the Netherlands. Near universal initiation of intensive care (US) compared with selective initiation of intensive care (Netherlands) was associated with 24.1 additional survivors per 100 live births, 7.2 additional cases of disabling cerebral palsy per 100 live births and a cost of 1,372 additional ventilator days per 100 live births. Unfortunately this study did not report on less disabling neurological complications or other sequelae.

Discussion

A newborn has a right to good quality of life, not simply a right to life. Imposing prolonged suffering upon a child, justified under a belief in the sanctity of life, reflects clinicians' or parents' beliefs rather than the best interests of the newborn. Parents, clinicians and the community as a whole must conclude that their obligation to a newborn is to act in their best interests. In a case where tests indicate a prognosis of severely disabling cerebral palsy, the right action ought to be to withdraw treatment and institute palliative care measures.

Orzalesi *et al.* examined four ethical principles as they apply to extremely premature newborns. [14] These principles, given equal priority, tend to conflict with each other. Presented with a neonate who does not possess autonomy, priority must be given to the autonomy of the surrogate decision-makers (the parent/s and treating clinicians). Beneficence and non-maleficence prescribe the duty to benefit and not to harm other people. They must be viewed in terms of the larger picture. Most diagnostic and therapeutic acts involve some form of harm in the short-term. Therefore beneficence in the long-term must take priority. With increased diagnostic and prognostic reliability, and assuming one views severe disability as an undesirable trait, the initiation of often painful treatment to prolong the life of a child with significant likelihood of severe disability would be harmful and clearly contravenes this principle. [14]

Justice in this situation implies fairness of treatment from an economic standpoint, in terms of allocation of resources where resources are finite. [14] It costs AU$2,740 per day to keep a baby alive in a neonatal ICU in Australia. In a large number of cases, this cost may increase substantially over time as a result of the patient's developmental conditions relating to prematurity. [23] It would be wrong to keep a child alive with a very poor prognosis when these resources could be used to keep children with the prospect of a reasonable life alive. When 1.4 billion people live on less than US$1.25 per day, and thousands of healthy babies are born each day but go on to die before their first birthday due to preventable disease, one cannot morally justify spending such large amounts of money on a child of borderline viability. Approaching the study by Lorenz *et al.* from this utilitarian perspective, it is difficult to justify an additional 1,372 ventilator days which only result in 24.1 additional survivors per 100 live births, a significant number of which will have neurological sequelae. One can easily recognise that beds made available for newborns with a better chance of survival (such as those born at >25 weeks) would result in more survivors, with a better long-term prognosis.

Further on the principle of distributive justice, there remains significant geographical inequality with premature newborn care. A notable disparity exists between survival and disability outcomes between newborns born in tertiary neonatal centres and those born in rural and remote centres, a relevant point in a large country such as Australia. [7]

Conclusion

The decision to resuscitate extremely premature newborns is a relatively new ethical dilemma brought about by advances in neonatal intensive care within the last half century. Continuing medical and technical advances in neonatal intensive care will result in ongoing revisions of current medico-legal and ethical guidelines. Decision-making regarding refusal, initiation and withdrawal of intensive care will remain a process which occurs between doctors and parent/s, taking into account the newborn's best interests, parental autonomy and the clinical judgement of the treating neonatologist. To determine the correct moral decision, the neonatologist should consider their duties of beneficence and non-maleficence and the shared duty of distributive justice.

A paradigm change to a more palliative, holistic approach is, in many places, already embedded in the neonatal ICU. This necessarily incorporates physical, psychological and spiritual aspects of the dying process that the infant and the family are experiencing. Neonatologists who are not comfortable with this approach and attempt to save every child born before 25 weeks are doing a disservice to the patient, their family and the community in general.

Opportunism must not override compassion. Whilst there are the knowledge, skills and appropriate technology available to keep an extremely premature newborn alive, it would be prudent to consider the short- and long-term ramifications of such a decision on the child, their family and the health care system.

The widely practised approach of treating all potentially-viable newborns is resource intensive and will result in short- and long-term physical, psychological and emotional distress. An alternative approach involving default non-initiation of treatment in newborns born under 25 weeks gestation, with treatment being the exception rather than the rule, would benefit from wider discussion and debate.

Conflict of interest

None declared.

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Reflections on an elective in Kenya

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"*In Africa, you do not view death from the auditorium of life, as a spectator, but from the edge of the stage, waiting only for your cue. You feel perishable, temporary, transient. You feel mortal. Maybe that is why you seem to live more vividly in Africa. The drama of life there is amplified by its constant proximity to death.*" – Peter Godwin. [1]

Figure 1. *Baby hospitalised for suspected bacterial pneumonia.*

Squeezing into our rusty *mutatu* (bus), we handed over the fare to the conductor, who returned to us less than expected change. In response to our indignant questioning, he defiantly stated, "You are *mzungu* (white person) and *mzungu* is money." This was lesson one in a crash course we had inadvertently stumbled into: "Life in Kenya for the naïve tourist." More unsettling than being scammed in day to day life, however, was the rampant corruption in the hospital and university setting.

We completed our placement at Kenyatta National Hospital, the largest referral centre in Kenya, with 1,800 beds, 50 wards and 24 operating theatres. I was based within the paediatric ward and paediatric emergency department.

According to the Corruption Index 2010, Kenya has the dubious honour of being the tenth most corrupt country in the world; [2] we soon witnessed this corruption first hand. Unable to understand Swahili, it took us some time to realise that the patients' relatives waiting in long, reaching lines were actually trying to bribe myself and the other exchange students to see them first, apparently common practice in the hospital. Local medical students at the hospital told us that there were some nursing and medical staff who would provide "better care" and more medication for some under-the-table money. One student told us that he was yet to be allocated a parking permit as he had not bribed hospital administration. In December 2010, shortly before our arrival in Nairobi, the Kenyan government admitted that up to one-third of the national budget is lost to corruption annually. [3]

While it is easy to condemn corruption amongst relatively well-off government officials, it is much harder to begrudge the average Kenyan for participating in this rotting system by applying my moral standards, born high in the comforts of a first-world ivory tower. Doctors included, Kenyan medical staff are paid shockingly low wages in comparison to Australia, despite tougher working conditions including long hours and exposure to an array of infectious tropical diseases, not to mention HIV.

Another eye-opening aspect was the low expectations of healthcare outcomes. While I had expected this to an extent, it is an entirely different experience to witness this in person. In a setting where there is no sphygmomanometer, one cannot expect fastidious hygiene and infection control. Babies shared intravenous fluids, with five infants receiving fluid from the same bag, while children with tuberculosis would be placed next to immunosuppressed leukaemia patients. We saw children with large abdominal masses and heart murmurs who received no further imaging or investigations because they could not afford treatment, regardless of the diagnosis.

Figure 2. *The sink in an isolation room for immunocompromised children.*

On one especially shocking morning we found an intern unsuccessfully attempting to resuscitate a four year-old child. The intern casually stated that he could not find the intubation equipment and thus could only administer oxygen via a bag and mask, while the child's mother was on the floor, sobbing next to her dying son. The consultant walked past the scene, not giving it another glance, and continued on the ward round. Death felt commonplace and omnipresent in every corner of the hospital, like the table in the back of the emergency department where I had directed a mother to change her baby's diaper, until a nurse shooed us away, hissing that it was reserved for the bodies of the deceased children which were sure to pile up by the day's end.

Standards of care and expectations of health are much lower, which is not altogether surprising in a nation in which the average life expectancy is 55. [4] The goal for most is survival, and optimal long term health is a luxury many cannot afford. A clear example of this is the wide usage of chloramphenicol. The drug is cheap and effective, but has with it the fatal side effect of aplastic anaemia. It is for this

reason that oral chloramphenicol is no longer used in the developed world. [5]

Whilst Kenyatta is a public hospital, patients were still charged for medical care. Inevitably, many of the families we saw during our stay were unable to afford treatment. Relatives were forced to leave their children, basically as ransom, whilst they returned to their villages to try and raise money. Sadly, this meant that the now-healthy children would remain at hospital and would thus be exposed to a multitude of pathogens, often falling sick again, and on several tragic occasions, succumbing to these nosocomial infections.

Figure 3. *A ward in the paediatrics department. Single cots were usually shared between patients and their parents.*

I do not mean to imply that our time at Kenyatta was completely disheartening. Doctors there have been known to cover the cost of their patient's treatment themselves. The hospital also helps fund patients whose needs are especially great. I was amazed by some doctors who kept so calm while facing long lines of patients, many of whom were desperately ill. Most inspiring of all were the children themselves, playing in dirty corridors, their faces lighting up when they saw us, calling out, "*mzungu*, *mzungu*!"

I left Kenya angry and frustrated from the corruption I witnessed and experienced on a daily basis, as well as with the abject poverty, which acts both as the cause and effect of the corruption. At the same time, I could not pinpoint the subject of my frustration: the doctors, who were doing the best they could under the circumstances? The entire African continent, grappling with dysfunction on multiple levels? Myself, for being born in a developed country? As I'm sure many of my final year colleagues agree, an elective in Africa is an amazing experience. It was hard to cope, however, with such blatant health disparity and the guilt I felt for being able to fly far away from Africa when my time there was complete. The beautiful children, parents and medical staff that we encountered are as much a part of Africa as its unrelenting problems, which urgently require solutions that I fear will not be in reach anytime soon.

Acknowledgements

Eunji Hwang for photography.

Gyo Suzuki for editing this submission.

Kenyatta National Hospital in Nairobi, Kenya and its paediatric staff and medical students.

Conflict of interest

None declared.

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A neuroanatomical comparison: Blumenfeld's *Neuroanatomy through Clinical Cases* vs. Snell's *Clinical Neuroanatomy*

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Joule is passionate about education, from both teaching and learning perspectives. He currently enjoys studying neurology and being involved in educational and peer tutoring programmes run by the Adelaide Medical Students' Society. In the longer term, he plans to incorporate the field of Medical Education in his future career.

Blumenfeld H. Neuroanatomy through Clinical Cases, Second Edition. Sunderland: Sinauer Associates; 2010.

RRP: AU$119.95

Snell, RS. Clinical Neuroanatomy, Seventh Edition. Baltimore: Lippincott Williams & Wilkins; 2009.

RRP: AU$107.80

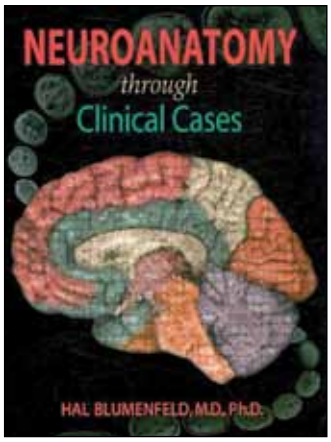
As stated by Sparks and colleagues [1] in their comparison of *Clinically Oriented Anatomy* and *Gray's Anatomy for Students*, studying anatomy can be a challenging endeavour. This is true even more so for the study of neuroanatomy, which many students find particularly overwhelming. In the neuroanatomy textbook arena stand two 'gold standard' textbooks: *Neuroanatomy through Clinical Cases*, by Hal Blumenfeld, and *Clinical Neuroanatomy*, by Richard Snell. Inspired by the aforementioned comparative anatomy textbook review in the previous issue of the journal, I ponder the question: Which neuroanatomy textbook is superior, the more established Snell or the newer Blumenfeld?

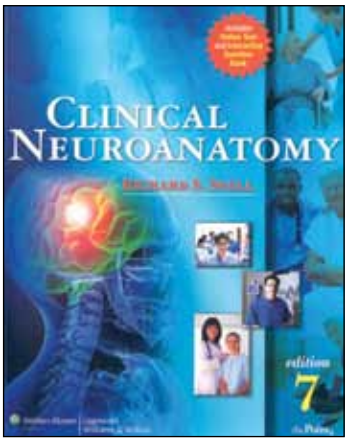
I begin my comparison with a consideration of their similarities. Both textbooks have a similar layout: after a few introductory chapters, they apply a quasi-regional approach to neuroanatomy, with chapters on the topics of the spinal cord, cerebellum, basal ganglia, and other major areas. This layout suits the beginner, with the introductory chapters at the beginning of each textbook providing a strong foundation from which to learn the more detailed material presented in the later chapters. Another great strength shared by both textbooks is the extensive use of radiological images which provide clarity of understanding that would not be achieved by illustrative diagrams alone. [1]

From here, however, the textbooks start to diverge. The first divergence is in terms of textual detail. Blumenfeld includes more rigorous explanations than Snell. Being less thorough makes Snell easier to read, but Blumenfeld's rigor tends to provide a more complete understanding of each topic. An illustrative example of this is in regards to learning the facial nerve (cranial nerve VII). Snell provides an effective yet simple description of the facial nerve in approximately three pages. In comparison, Blumenfeld's six-page-long description of the facial nerve contains more detail and more diagrams. It also includes a relatively detailed summary of facial nerve lesions, the corneal reflex and the jaw jerk reflex. While the number of pages devoted to a topic may be a rather crude measure of textual detail, one cannot ignore the fact that Blumenfeld, at an impressive length of 976 pages, is almost twice that of Snell's 560 pages. In the end, whether it is desirable to prioritise depth, or ease of reading, is up to the individual student, but I perceive the greater depth of Blumenfeld as generally preferable.

Another difference lies in the method by which the textbooks deliver the clinical relevance of the neuroanatomy described. Blumenfeld uses a combination of *Key Clinical Concepts* and *Clinical Cases*, whereas Snell uses a combination of *Clinical Notes*, *Clinical Problem Solving* and *Review Questions*.

In Blumenfeld, each Key Clinical Concept is a concise summary of a particular symptom, condition, syndrome, or disease. For example, *5.3 Key Clinical Concept: Elevated Intracranial Pressure* details the pathophysiology behind raised intracranial pressure, the mechanisms





leading to the relevant clinical symptoms and signs (headache, altered mental status, nausea/vomiting, papilloedema, visual deficits and Cushing's triad), and the appropriate interventions. After explaining the *Key Clinical Concepts*, the *Clinical Cases* are introduced. These begin with a short case presentation of a patient's presenting complaint, history and physical examination, followed by several questions. Blumenfeld then works through the case, discussing the key symptoms and signs, and the resultant clinical course (usually including investigations and management). For example, *Case 6.1 Sudden Onset of Right Hand Weakness* describes a 64-year-old man presenting with right hand weakness following cardiac arrest. The key symptom and sign is then discussed, as well as the subsequent clinical course and neuroimaging. There are a total of 121 *Clinical Cases* in Blumenfeld.

In Snell, the *Clinical Notes* are brief explanations of clinically relevant concepts. For example, the *Clinical Notes in Chapter 2: The Neurobiology of the Neuron and the Neuroglia* provide short paragraphs on *General Considerations*, *Reaction of a Neuron to Injury*, *Axonal Transport* and the *Spread of Disease*, *Tumours of Neurons*, and so on. These *Clinical Notes* are then supplemented by a *Clinical Problem Solving* section, which mostly contains scenario-type questions, and by a Review Questions section, which mostly contains multiple-choice questions. These sections are followed by their respective *Answers and Explanations*.

In many ways, the *Key Clinical Concepts* present in Blumenfeld and the *Clinical Notes* in Snell are very similar, but again, Blumenfeld tends towards greater depth. Furthermore, neuroanatomy is traditionally described as a dry and boring subject, and each *Clinical Case* provides an interesting and clinically relevant context to learning that generally aids retention and understanding of core concepts. On the other hand, Snell's *Clinical Problem Solving* and *Review Questions* are an excellent resource for testing one's knowledge and for exam preparation, and the utility of these questions as such a resource should not be underestimated.

Discussion of Blumenfeld would not be complete without mention of the neuroexam.com website. [2] The website is specifically designed by Blumenfeld to complement his textbook. The videos on the website are free to view, and anyone with internet can access them. However, the effectiveness of this resource can naturally be maximised by concurrent use of Blumenfeld's textbook, whereas it provides Snell's textbook a less synchronous accompaniment.

Overall, I feel that Blumenfeld is more detailed and therefore easier to understand as the student can more fully understand each topic. I also believe that the information presented in Blumenfeld is easier to retain due to the very clear 'bedside' relevance of the neuroanatomy taught as compared to Snell. However, Snell provides a succinctness which is excellent for a general overview of neuroanatomy and may therefore be more suitable for junior students. So which textbook is the winner of the battle in the neuroanatomy textbook arena? The ultimate decision lies with you, but for the reasons I have outlined, I recommend Blumenfeld.

Conflict of interest

None declared.

References

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Tumaini

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Sarah, originally from Newcastle, is interested in paediatrics, emergency medicine and gastroenterology. Her elective in Tanzania has sparked her enthusiasm for public health and healthcare delivery in developing countries. Her research in patients' knowledge of the contraceptive pill has recently been published in the Journal of Women's Health.

This photograph was taken during a four week elective placement at Ilula Lutheran Hospital, located in the southern highlands of rural Tanzania, East Africa. It emphasises the innocence and resilience of this country's generous, kind people.

Ilula Lutheran Hospital is a 70-bed facility with a geographically broad service area. Patients often travel long distances to seek attention at the facility, and present most commonly with conditions such as malaria, complications of HIV, malnutrition, trauma, burns, respiratory and diarrhoeal illnesses, often in their advanced stages.

This photo was taken while visiting a village on an HIV outreach clinic. Nurses and doctors attend villages monthly to diagnose new patients, dispense anti-retroviral therapy and perform general check-ups. The rate of HIV infection in the Ilula area has not been accurately measured; however, the infection rate has been estimated at approximately 20% in the general community and 50% amongst hospital inpatients. The day this photo was taken, the nurses and doctors were helping villagers form a support group to facilitate communication between them and the hospital, to encourage new patients to seek help and to give existing patients a support network to aid with compliance. This little boy was shy as he hid behind the skirt of his HIV-positive mother. The support group was named *Tumaini* – hope.

This photo was the winner of the 2011 Medical Students' Aid Project photo competition. MSAP is a not-for-profit organisation run by medical students from the University of New South Wales. MSAP's goal is to send targeted aid to developing world hospitals visited by UNSW medical students on their elective terms. This is done through collecting donations of equipment from hospitals and doctors around the state, as well as fundraising to purchase additional equipment and arrange for delivery of these supplies. To ensure that the equipment sent is appropriate and useful, the hospitals are asked to compile a "wishlist" of required supplies. In addition, MSAP also educates medical students on issues associated with global health throughout the year. To find out more, and how you can help, visit www.msap.unsw.edu.au today!

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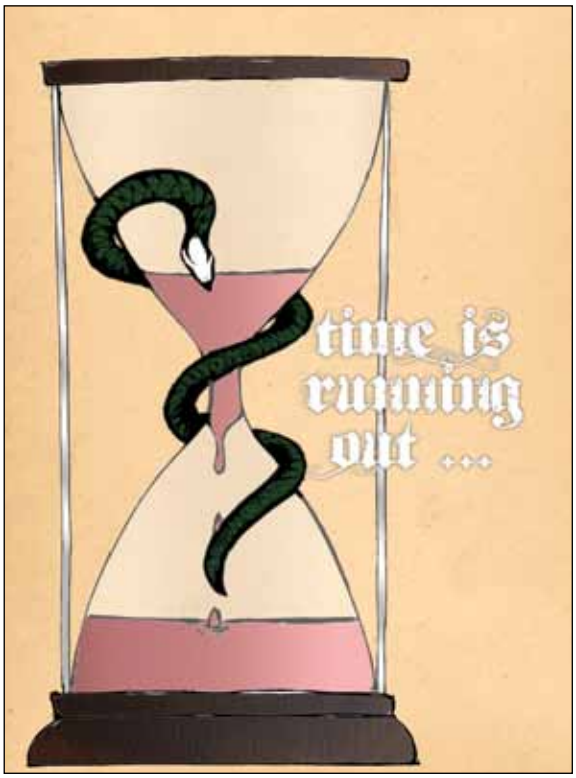

Front cover photography by David Pham from University of New South Wales. Alternate cover illustration (above) by Sina Fathieh from University of Newcastle.

Design and layout
© 2011, Australian Medical Student Journal
Australian Medical Student Journal, PO Box 792, Kensington NSW, 1465
enquiries@amsj.org
www.amsj.org

Content
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ISSN (Print): 1837-171X
ISSN (Online): 1837-1728

Printed and bound in Australia by Ligare Book Printers.

The Australian Medical Student Journal is an independent not-for-profit student organisation.

The Australian Medical Student Journal can be found on EBSCOhost databases.

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