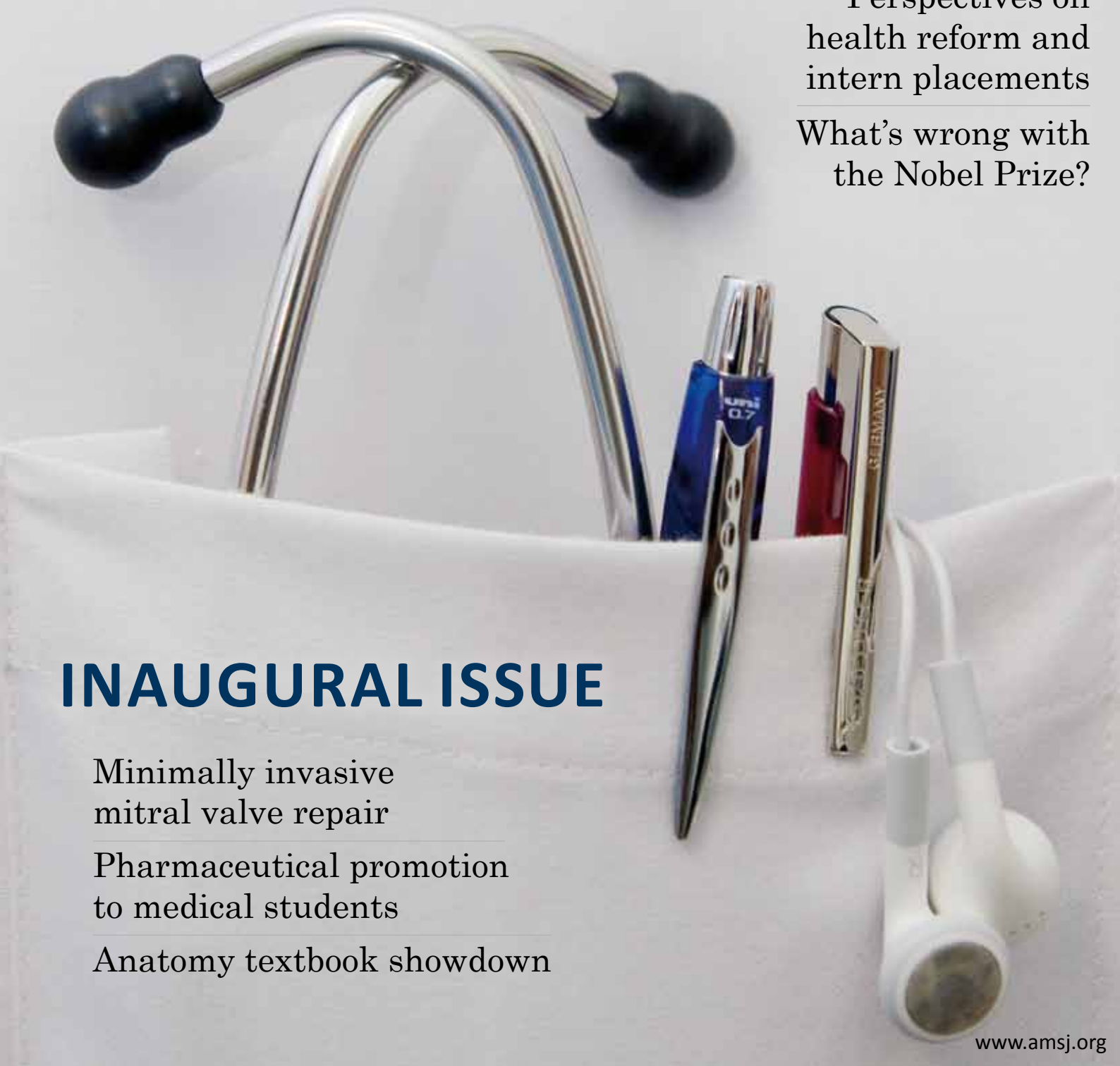
Volume 1, Issue 1 | April 2010

Australian Medical Student Journal



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Australian Medical Student Journal

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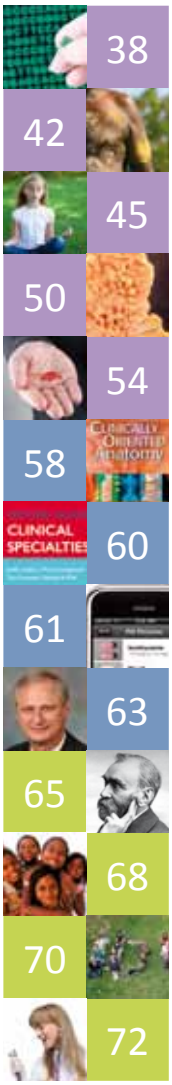

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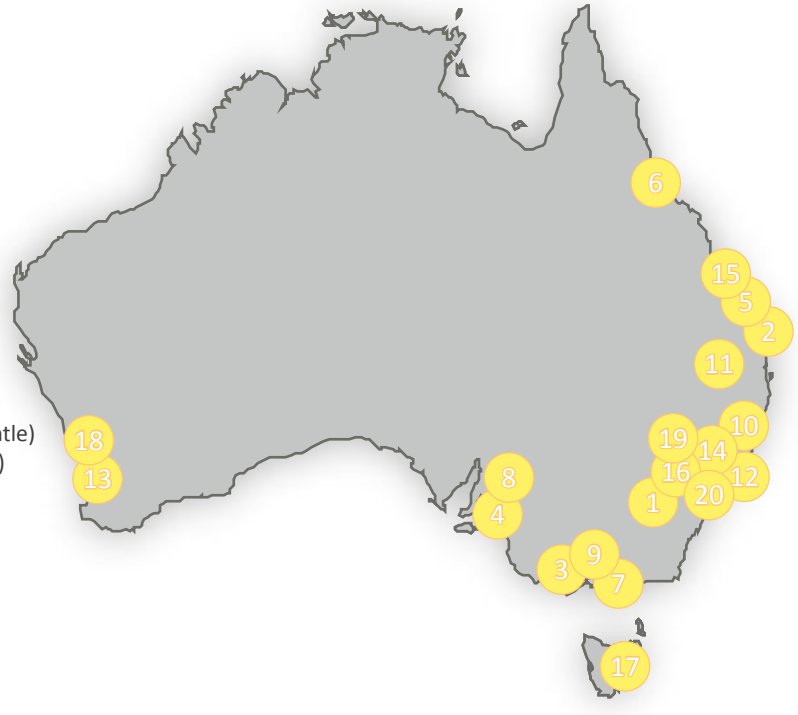

The Australian Medical Student Journal is born

Matt Schiller
Chair, AMSJ
Fifth Year Medicine/Arts, University of New South Wales

It is a delight to welcome you to the inaugural issue of Australia's new national medical student journal.

As you will no doubt discover, this first issue of the AMSJ really is a showcase of the talent, passion and achievement of medical students from across the country.

In recent times, medical education in Australia has seen a paradigm shift to self-directed learning and evidence-based medicine, and medical students themselves have become an increasingly diverse cohort with a wide range of backgrounds and interests. The AMSJ is in many ways a response to the corresponding need for avenues of expression.

In less than a year, the AMSJ has developed from an idea to a reality of previously unimaginable quality and scale. Every stage in the journal's development has been somewhat of a leap into the unknown. One of the critical hurdles for the concept was always going to be the response in terms of submissions. We were overwhelmed with both the quality and quantity of what was received, with the vast majority of Australia's twenty medical schools being represented among the submissions. The only regret is that only a small proportion were able to be published in the inaugural issue. Ultimately, it is the authors who have made the AMSJ a success, and will continue to do so.

The AMSJ has been a challenging balancing act in many respects. While we wanted to steer well away from being another student magazine, we did not want to be constrained by all of the typical expectations of a biomedical journal. We are not the first such journal in the world, however we found that the whole concept of a 'student medical journal' still needed to be defined; such a journal needs to be student-friendly for both authors at one end, and readers at the other.

From the perspective of student authors, we aimed to provide an unintimidating forum that could be a stepping-stone into the world of academia. While all academic articles underwent rigorous internal and external review processes, being anonymously peer-reviewed by at least two experts in their particular field, a central concern was to be as constructive as possible with any author feedback. A student journal needs to avoid the type of harsh uninformative rejections that are sometimes met with in existing journals. The AMSJ offers opportunities for a wide variety of styles, and for more general-interest articles that may not find a place elsewhere. As such, in this issue, you will find what you are familiar with in existing journals, such as review articles, original research, and case reports. However, you will also find many pieces that traverse the traditional boundaries, such as reviews of student resources, career pieces, and a host of feature articles.

From the perspective of you, our readership, the central concern was to be relevant and interesting. There is little use in publishing articles, regardless of the excellence of the research behind them, if they are of an extremely specialised nature and of no appeal to the vast majority of medical students. By the same token, we needed to publish articles that could extend students beyond the limits of standard medical curricula.

Matt Schiller

None of this would have been possible without our extremely dedicated volunteer staff of twenty-two students, to whom I offer heartfelt thanks and congratulations. As we all quickly learned, being involved in a totally new professional organisation is no easy task – every single process has to be designed from the ground up, without the luxury of a predecessor to lean on for advice. But at the same time, this has imparted an amazing degree of creative freedom that everyone found most rewarding.

There are a host of other people who have made this venture possible, including the generous and dedicated academics and clinicians who became peer-reviewers, our sponsors, medical societies from around the country, and the UNSW Faculty of Medicine, particularly Dr. John Hunt.

If what follows in the next seventy or so pages represent what is possible for an inaugural issue, then the future for the AMSJ certainly seems bright. I would encourage any student who reads this issue to take inspiration from their colleagues' work published in these pages and think of how they could contribute to future issues, and indeed to the field of medicine in general.

A group of AMSJ staff members at a meeting in Febuary, 2010.

A promising future for youth mental health

Prof. Patrick McGorry
Australian of the Year, 2010
Chair in Youth Mental Health,
University of Melbourne

For the last 27 years, Prof. McGorry has been at the forefront of the promotion of youth mental health and early intervention, not only in Australia, but worldwide. A psychiatrist by training, he has become the ninth in a series of distinguished individuals in the field of medicine to be named Australian of the Year since the award's inception in 1960.

We have good reason to be concerned about the mental health of our young people.

In Australia, mental health issues account for 55% of the total burden of disease in those aged between 15-24 years, with depression, anxiety and substance misuse being the most prevalent problems in this age group. [1,2] Furthermore, epidemiological evidence tells us that over 75% of people who suffer from a mental illness experienced their first episode by the age of 25 years. [3] Given the exquisite developmental sensitivity of this period of life, when psychological, social and vocational pathways are being established as part of the transition to independent adulthood, it is not surprising that mental disorders, even relatively brief and mild ones, can disrupt and disable, seriously limiting or even blocking a young person's potential. Ample evidence shows that mental ill-health in young people is associated with high rates of enduring disability, including school failure, unstable employment, poor social and family functioning, which all too often lead to a spiral of disability and disadvantage that becomes difficult to reverse.

As a society, we cannot afford to ignore the human, social and economic consequences of this situation. A recent report by Access Economics has estimated that in 2009, the financial cost of mental illness in Australians aged between 12 and 25 years was $10.6 billion, with 70.5% of this due to the costs of lost productivity due to lower employment, absenteeism and premature death. Furthermore, the value of the loss in well-being (disability and premature death) was estimated at a further $25 billion. [4] We need to invest in our future, and clearly, investing in youth mental health makes good sense: a strong focus on young people's mental health has the capacity to generate greater personal, social and economic benefits than intervention at any other time in a person's lifespan. Put simply, mental health equates with national wealth, in the broadest possible sense.

Fortunately, there is a growing movement that aims not only to raise awareness of this crying area of unmet need, but also to redress it. In the early 1990s we began to promote the idea that intervention in the very early stages of the development of a mental illness was the most effective strategy to reduce the burden of disease created by these disorders. Intervening early to stop the progression of a mental illness should also prevent the accumulation of collateral damage to educational, social and vocational functioning associated with the evolution of the illness. Evidence supporting this proposition has been building steadily over the last decade, and with this progress, it is now accepted at both the State and Federal Government levels, as well as within the wider community, that major reform and significant investment is required in mental health care in Australia, and indeed world-wide.

As Australian doctors, present and future, we live in exciting times. We have reached the tipping point; reform is inevitable, and indeed, the first steps have been taken. A career in psychiatry has always offered benefits such as real contact with patients, rewarding work, intellectual stimulation, interesting research questions and the possibility of maintaining a good work/life balance, but now Australia's psychiatrists have the potential to be part of a social climate change not only here in Australia, but also world-wide. The need is only too real, and the potential to address it has never been better. As Australia's doctors of the future, an exciting career option beckons you: consider psychiatry, and make a real difference to our future.

Prof. Patrick McGorry

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From the Prime Minister

The Honourable Kevin Rudd MP
Prime Minister of Australia

Congratulations on the inaugural issue of the Australian Medical Student Journal

As Australian medical students, you are the future medical workforce studying to shape the health and well-being of the next generation of Australians.

This is an exciting time to join the medical profession, in the midst of the biggest reform to the health and hospital system since the introduction of Medicare. Recently, I announced the Government's National Health Reform Plan. The Plan is based on a vision that future generations will enjoy world class, universally accessible health care — the quality of care that has helped deliver Australians the third longest life expectancy in the world.

The Reform Plan will build on the strengths of our current health system, such as access to primary health care through Medicare, and free public hospital treatment for public patients. We want to improve public hospital and primary health care services, since these services underpin Australia's entire health system.

Most importantly, the Reform Plan will harness and build on the skills, experience and ingenuity of those, such as yourselves, who work on the front line of our health and hospital system.

Yours is the work of saving lives – restoring, curing and protecting the young; the old; rich and poor alike – through life-changing treatments, discoveries and breakthroughs. It is work that I appreciate. Work that all Australians appreciate.

Australia needs students such as yourselves to achieve the breakthroughs in medical science that prevent disease, cure illnesses and deliver a better quality of life. I wish

each of you all the very best for your future endeavours, and I commend you for choosing a profession which is so important to the future of our nation.

From the Minister for Health and Ageing

The Honourable Nicola Roxon MP
Minister for Health and Ageing

The Rudd Government knows that Australia needs an effective, streamlined and integrated health workforce if it is to meet the challenges our health system faces in coming years - including the ageing of our population and an uneven distribution of health services.

We recognise that increasing numbers of medical students and junior doctors are coming through the system and we need to ensure that students are provided with quality clinical education and training. Since our election two years ago, the Rudd Government has made significant progress to achieve these goals.

Accordingly, we led the major health workforce reforms agreed to by the Council of Australian Governments in November 2008 and formalised in the National Partnership Agreement on Hospital and Health Workforce Reform. This $1.6 billion package, of which the Australian Government will contribute $1.1 billion, is the largest investment in the health workforce ever made in Australia. This landmark investment includes $1 billion for the clinical training of undergraduate students. Importantly, an agreement was also struck with the states and territories agreeing to provide intern places for students with Commonwealth-supported places.

Another key measure in the package is the establishment of Health Workforce Australia (HWA), an independent, truly national body that will work across the health and education sectors to deliver the right number of high quality health graduates. HWA will support workforce reform initiatives: of particular interest to medical students will be its role in funding, planning and coordinating undergraduate clinical training across all health disciplines and in a variety of settings and locations. It will also provide support for an international recruitment program and capital infrastructure, including for simulated learning environments, innovative clinical teaching and training initiatives and rural clinical school programs.

We are facing a time of great change for our health system. I recently joined the Prime Minister to announce a vision for the future that will be the most significant health reform since the introduction of Medicare. Simply put, this will mean a national hospital network, funded nationally and run locally. The second plank in this reform is that we intend to produce a health workforce that complements and supports this vision – and you, as medical students, are a vital part of that endeavour.

On March 15, the Prime Minister and I announced that the Rudd Government will invest another $632 million to train a record number of doctors - to tackle doctor shortages, expand capacity and deliver better health and better hospitals. This investment will deliver an additional 5,500 new or training General Practitioners, 680 medical specialists, and 5,400 pre-vocational general

practice program training places over the next ten years. These major investments will meet projected shortfalls, and help reduce pressure on hospitals by improving access and availability of GP and specialist services.

When you have completed your training, we want you to be proud to be joining the Australian health workforce. So we intend to build for you, and all Australians, a health system that is not only able to cope with the challenges ahead, but do so while offering even better quality, even better access, and even greater choice.

Congratulations on the first edition of the Australian Medical Student Journal and best of luck to all readers with their studies.

Medical training: A key part of health reform

Dr Andrew Pesce
President
Federal AMA

The AMA is very honoured to be part of the inaugural edition of the Australian Medical Students Journal, and to be involved in the work and thinking of the next generation of medical professionals.

Medical education and training is a key part of any health reform agenda. Without a quality future medical workforce, no health reform will be a success. The AMA keeps reminding Governments of this important fact.

The Commonwealth's recent health reform announcements are an opportunity to improve and to define more clearly the funding arrangements (and therefore responsibility) across the stages of medical education and training. Like all parts of the health system, clinical training in particular has been caught up in blame shifting. The Commonwealth decides on intakes to medical schools, but the States and Territories provide the lion's share of clinical training in the public system. This means that while the Commonwealth has embarked on a massive increase in medical student numbers since 2004, there is no guarantee that the States and Territories will supply all the pre-vocational and vocational training positions in public hospitals that are needed for the increased graduate numbers.

The Commonwealth's plan to identify and fund 60 percent of the costs of training in public hospitals may give the Commonwealth more say in making this happen. The Commonwealth has also recently announced a significant investment in training places. This funding provides for more pre-vocational General Practice placements, more GP vocational training places and more specialist training places in private, community and rural settings. This is great news and is in line with the proposals put forward by the AMA.

States and Territories must now play their part and fund more prevocational and specialist training positions in their public hospitals to make sure that we can give all future graduates a training position. We need to make sure there is the right level of investment in the infrastructure and resources to support these places; quality supervision is key to the successful roll out of these places.

The AMA met with the Minister for Health and Ageing in March to discuss clinical training issues – specifically infrastructure and resources for clinical training, including the AMA proposal for the Government's new body, Health Workforce Australia, to take a strong role in providing for pre-vocational and vocational training. Currently it only provides for undergraduate clinical training.

Health Workforce Australia funding should supplement the efforts of the States and Territories by funding discrete projects that will boost training capacity across the system. This includes funding for dedicated teaching and training time for senior clinicians, the development of innovative training programs for interns, professional development programs to enhance the teaching capacity of junior doctors, and extra prevocational training positions in community settings.

Importantly, the Government has recently agreed to a continued and expanded role for the Medical Training Review Panel (MTRP). The MTRP has a key role to play in monitoring and reporting on the availability of clinical training places, particularly for pre-vocational doctors such as interns, given the significant increases in medical school places in Australia. The AMA has strong representation on the MTRP.

While there is positive movement by the Government with regards to numbers, we need to make sure that the quality of medical education is not compromised. There is a very real threat to this as Governments attempt to do more with less.

Dr Andrew Pesce

While the AMA appreciates the need to find innovative ways of teaching, methods must respect that quality clinical placements and mentoring by senior doctors must remain the cornerstone of medical education.

We need to constantly remind politicians that it is bad policy to reduce the quality of medical education and training or seek to replace the central role of the doctor with lesser-qualified health workers.

The AMA will be running with many messages this election year – just as we have been doing already on the health reform agenda. Boosting quality medical education and training will be one of those messages.

An evidence-based approach to representation

Ross Roberts-Thomson
President, Australian Medical Students' Association (AMSA)
Sixth Year Medicine (Undergraduate), University of Adelaide

Research is an important part of a medical education and to be able to accurately interpret, contribute to and even publish research is something all medical students should be able to do.
Thus, it is a pleasure to be able to welcome you to the first edition of the Australian Medical Student Journal.

Medical students have made some significant discoveries over time, including heparin, insulin, Ether anesthesia and even the sinoatrial node. Furthermore, a significant proportion of medical students would like to have research as part of their future career. Thus it makes sense for medical students to have and run a journal to showcase their work.

Over the past number of years, AMSA has conducted the AMSA Medical Education Survey. This survey looks at what medical students think about medical education in Australia and what their future intentions are. Governments, non-government organisations, lobby groups, universities and researchers around the world have used these data for various purposes and they are, of course, infinitely useful for AMSA itself.

In the current paradigms of science, politics, and education, being merely a representative body is no longer sufficient. Representation must be backed by robust evidence and thus AMSA must be the true authority on medical students if it is to be successful into the future. It is in this light that AMSA is pursuing a more evidence-based approach to medical student advocacy, something we like to call Evidence-Based AMSA.

As part of this initiative we are looking to collect qualitative as well as quantitative and anecdotal evidence to help further our advocacy and shed light on issues affecting medical students. Evidence-Based AMSA will be conducted in consultation with epidemiologists and education experts. It will allow us to better direct our arguments on issues affecting medical students, and subsequently enhance AMSA's influence over Governments, university institutions and non-government organisations.

AMSA will also be forming ties with one of the world's biggest pools of data on medical students - the Medical Deans of Australia and New Zealand Medical Student Outcomes Database (MSOD). The MSOD collects a variety of data including where medical students come from, what rotations they do and their respective career intentions. The Medical Deans Longitudinal Tracking Project even follows these students beyond university to see where they actually end up practicing.

Ross Roberts-Thomson

Linking the AMSA Medical Education Surveys with the MSOD and Longitudinal Tracking Project provides a more solid foundation upon which to base our conclusions and recommendations, and this partnership is one AMSA is extremely excited about.

Finally, to give students the opportunity to publish and be involved in the running of a journal such as this is a great initiative and I very much look forward to future editions of the Australian Medical Student Journal.

Getting excited about Evidence-Based Medicine

Henry Goldstein
Fourth Year Medicine (Graduate)
University of Queensland

Bryan Hawarden
Fourth Year Medicine (Graduate)
University of Queensland

Significant emphasis is placed upon Evidence-Based Medicine (EBM) during medical school, resulting in student responses ranging from apathy to consternation.

Students take home the importance of systematic reviews and highly populated, well-powered trials, to the apparent exclusion of all else. That these trials often have landmark effects is not disputed, but there remains a paucity of data for many aspects of clinical practice. EBM is well equipped to handle this and hence it is worth re-emphasising the principles at the core of EBM.

In a well known BMJ Editorial, Sackett et. al. defined EBM as "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients". [1] A core principle that is seemingly becoming confused in medical education is that EBM involves utilising the best available, not necessarily the best possible, evidence.

It is essential medical students understand that EBM consists of three strands: several levels of published research, core scientific knowledge, and individual clinical experience. Whilst landmark trials, such as the S4 trial, [2] are easy for students to appreciate as quintessential EBM, smaller general publications, such as John Murtagh's Practice Tips, [3] equate to a distilled clinical experience that cover many areas of practice and should certainly be considered part of the EBM framework, particularly for students who have limited personal clinical experience.

The challenge is to successfully integrate EBM's three strands into clinical practice, particularly in scenarios where there is insufficient evidence in one area or even disagreements between data. In these situations, it is imperative to understand EBM's hierarchy of evidence and to critically appraise evidence; both of which require a sound understanding of the scientific method.

To achieve an optimal outcome in scenarios with conflicting or limited evidence is the hallmark of good EBM practice. As more data is gathered, disagreements are resolved and gaps filled. However, today's patients cannot wait for this to occur and medical students must develop thorough knowledge of EBM, including statistical analysis and philosophy of science, to allow them to confidently deal with such occurrences.

EBM lies at the core of modern medical practice; we who become doctors also become scientists. Our clinical decisions, based on experience and core knowledge, are moulded by the guiding hand of research.

Indeed, it is our duty to integrate the strands of EBM to ensure the best possible outcomes for patients. We applaud the AMSJ on its inauguration as a vehicle to encourage medical students into well-rounded, evidence based clinical practice.

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International medical students: Interned by degrees

Matt Schiller and Timothy Yang
Editors-in-Chief, AMSJ
Fifth Year Medicine (Undergraduate), University of New South Wales

The progression from university to the workforce in medicine is not comparable to any other discipline or profession.

An internship is essentially an extension of a medical degree, and the degree is redundant without one. The issue of the burgeoning numbers of Australian medical graduates, and the associated 'crisis' in intern placement availability, is currently the preeminent political issue for medical students. Increasingly, international students have been caught in the middle of the storm.

To put this situation in the proper context, one needs to look back to the late-1980s and 1990s. At this time, Australia was seen as being oversupplied with doctors in general. There was a strong policy reaction to this sentiment, which capped student numbers, and levied heavy restrictions on overseas-trained doctors. The turn of the century saw an abrupt turnaround in this attitude, as a different picture was painted about the country's long-term health workforce requirements. Temporary resident visas for overseas doctors grew from 664 in 1993-1994 to 1923 in 2001-2002. [1] On the graduate front, from around 2003, government policy has allowed international medical graduates to remain in Australia. [2] Given worsening projections for future workforce shortages, one could be forgiven for thinking that this was seen as the start of a norm that would continue indefinitely. While incoming international students were never given a guarantee of placement after graduation, until recently, it was often implied that this would never be an issue.

Australia only had ten medical schools in 1999, whereas today we have twice this number. [3] International places have increased as a proportion over this time. In 2002, 161 international students graduated from Australian medical schools, representing 11% of total graduates. This year, the number is predicted to be 423 students, or 16% of the total. This is as high as 34% at one institution. [4] Unfortunately, while governments eagerly and justifiably expanded the numbers of medical places at universities, this was not matched by sufficient planning for long-term doctor training. Consequently, last year, many graduates had genuine cause for concern about receiving an intern placement. However, just because we have a bottleneck of medical graduates does not mean that we have an oversupply. Make no mistake; the future of our health system needs every single graduate we are producing. Although we are dealing with unprecedented numbers, the training system needs to come to terms with this reality as soon as possible.

Even domestic Commonwealth-supported students have had reason to worry until the Australian Health Ministers' Conference this February, when they were given a guarantee of training places for the foreseeable future. This is to be achieved by doubling the undergraduate clinical training subsidy across all states for 2010-2011, with the annual commitment totalling $140m nationally. [5] While this is a very positive and encouraging step forward, it excludes many potential future doctors.

For international students, there are no guarantees. Worse still, some international graduates from certain Australian medical schools would not even be able to gain an internship-equivalent in their home country. One cannot underestimate the perspective of our international colleagues – after spending a fortune on living expenses and university fees, being told that they will not be able to continue their training in the country where they graduate. For some, continuing their training anywhere may be extremely difficult. This is the frightening scenario that many are now facing.

It is not a well-kept secret that many medical faculties around the country are heavily reliant on international students and their fees to fund medical programs. Can we justify milking international students for their dollars, followed by abandonment at graduation in favour of the colleagues whose degrees they subsidised? Furthermore, there is the possibility that the international student funding source could deplete if recent developments discourage new students from coming here.

Currently, governments spend enormous sums of money attracting and retraining foreign health workers. Admittedly, overseas-trained doctors are filling a more immediate gap in the system that is considerably further down the line of training than internships. This is no doubt necessary for the time being. Nonetheless, it seems senseless that we are prepared to spend such amounts bringing overseas-trained doctors into the country, but cannot bring ourselves to adequately train and retain doctors reared in our own top-class medical schools.

The ramifications extend beyond just international students. Local full-fee-paying students, who make up further 6% of medical graduates, are also excluded from the recent guarantee of training places. [6]

The challenge, of course, is not just to make places for more students, but to ensure that this does not affect the quality of teaching that all trainees receive. It is also critical that we do not simply replicate the mistakes of the past: we need to ensure that there is adequate downstream planning, not just more intern places. Recent government announcements about General Practice and specialist training places are encouraging in this regard. [7]

If governments consider international and domestic full-fee-paying students not worth retaining, then they should perhaps reconsider the approval of such medical places in the first instance. But for those already in our programs, this line of reasoning simply is not good enough. There is no adequate justification for any Australian-trained medical student being denied an intern placement. It is nonsensical to on one hand have a workforce shortage, and on the other hand be turning away the best long-term solution to that shortage. If someone is good enough to be trained in an Australian medical school, then they should be good enough to practice here.

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Can we predict when operating lists will finish in a regional Queensland hospital?

David Liu
Fourth Year Medicine (Graduate)
University of Queensland

David was a recipient of a University of Queensland (UQ) Research Scholarship in medicine for 2008-2009. In 2009, David presented at the Asian Medical Students' Association International Conference in Taiwan and was a UQ delegate at the Australian Medical Students' Association National Leadership Development Seminar in Canberra.

Winner of the Co-Op Bookshop Prize for Best Academic Article in this issue of the AMSJ

Background: Over-running operating lists are a common cause of same-day cancellations of surgery, while under-running operating lists are a common cause of wasted health resources due to the fixed costs of operating suites. The predominant cause of operating lists running off-schedule is not known, but it is believed that if due to booking problems, it should be possible to predict when a list will over- and under-run. **Aims:** To understand the prevalence of cancellations, over- and under-running operating lists in a regional Queensland hospital, and to test whether over- and under-running lists can be predicted. **Methods:** A sample of 120 operating lists was prospectively obtained and each list timed from start to finish. A predicted duration was calculated for each list by summing the average durations for each of the operations on the list (including anaesthetic and turn-over durations), derived from past surgical records. **Results:** Twenty-eight percent of lists suffered a cancellation, of which 79% were predicted to over-run their scheduled duration. Of the lists that did not suffer a cancellation, 45% over-ran, of which 84% were predicted; and 37% under-ran, of which 84% were predicted. **Conclusion:** The large proportion of predicted over- and under-runs support the hypothesis that booking problems are the main causes of operating lists running off-schedule, as opposed to other factors affecting surgical duration that the model would not have accounted for. This suggests that operating lists running off-schedule can potentially be avoided. Further study is warranted to investigate the reasons behind over- and under-booking.

Background

A problem in the management of operating schedules for hospitals is that operations do not always run to schedule. This can cause operating lists to over- or under-run their allocated time. In this paper, Pandit's [1] definitions for these terms were used:

- an over-run occurs when the actual duration of the list exceeds its scheduled duration by more than 20 minutes;
- an under-run occurs when the actual duration of the list is less than its scheduled duration by more than 20 minutes.

Studies in the United Kingdom show that the percentage of operating lists running significantly over scheduled time is between 21-53%, while the percentages of operating lists running significantly under scheduled time is between 33-39%. [1-3] There have so far been no similar studies conducted in an Australian setting.

A study from the United States compared operation durations with the time scheduled for those respective operations. Based on data of the 20 most frequently performed surgical procedures, it was found that for 31.8% of cases the actual case length exceeded the time scheduled for the procedure by 15% or more. For 23.1% of the cases, the actual case length was shorter than the time scheduled for the procedure by 15% or more. [4]

A number of studies have shown that over-running of operating lists is associated with cancellations of procedures. A study at a major tertiary hospital in Australia found that 13.2% of scheduled elective operations

were cancelled on the day of the procedure and the leading cause of cancellation (18.3%) was lack of theatre time due to over-running operating lists. [5] Similar studies in hospitals outside of Australia have had similar findings. [2,6-8]

Cancellations have a negative effect on quality of life for patients who have their operations cancelled, as well as those who are on elective surgery waiting lists. Patients who have their operations cancelled must live with a surgically treatable morbidity for a longer period of time, and have an increased risk of developing major depression within twelve weeks of their cancellation. [9] Cancellations also mean that patients who are on waiting lists for elective surgery may have their operations further delayed, meaning that they too must live with a surgically treatable morbidity for a longer period of time.

Under-running operating lists result in the under-utilisation of the total available operating theatre time. There are significant fixed daily costs of running an operating theatre, thus frequent under-running of operating lists is expensive. [10] In a health system with finite resources, cost-saving by minimising the incidence of operating list under-runs would mean that more funds would be available for use in other important areas of the health system. Avoiding under-booking of operating lists would also mean that sick patients can be treated earlier and waiting time for other patients on elective surgery waiting lists can be reduced. [11]

The aims of this project are to understand the prevalence of over- and under-running operating lists and cancellations (which are associated with operating list over-runs) in a regional Queensland hospital, and to test if over- and under-booking are the main causes of operating lists running over- and under-time, respectively. Intuitively, poor scheduling is a potential cause of operating lists running off-schedule, but the current literature has not established whether it is any more important than other demonstrated causes of prolonged or shortened surgical duration, such as patient factors, surgical techniques or skills of the anaesthetist or surgeon. [12-14] If booking behaviour does indeed represent the main reason why operating lists run off-schedule, it could potentially be modified to minimise over- and under-runs.

One method of testing this hypothesis is to investigate if it can be predicted when an operating list will run over- or under-time by adding the average durations of procedures on that operating list (taking into

account estimated time used for anaesthetics and turn-over between cases). Lists that predictably run off-schedule would likely to be due to scheduling errors (or intentional over- and under-bookings), while those that run off-schedule and cannot be predicted to do so through this model are likely to be caused by other factors that affect surgical duration.

Hypothesis

More than one quarter of the operating lists at the hospital will have a cancellation, and of those the majority would have been prospectively predicted to over-run. Around half of all operating lists will either over- or under-run, and that the majority of these would have been prospectively predicted to do so.

Methods

Using the regional Queensland hospital's Operating Room Management Information System (ORMIS), mean durations and turn-over times for all elective surgical procedures performed at the hospital from 1 March 2008 to 1 March 2009 were collected.

One hundred and twenty consecutive operating lists from the regional Queensland hospital between 1 April 2009 and 1 August 2009 were prospectively obtained. Only operating lists that contained operations or combinations of operations performed between 1 March 2008 and 1 March 2009 were included in this sample. A predicted duration was generated for each operating list by adding the estimated durations and turn-over times for the individual operations on that list. The possibility of using a regression model to increase the accuracy of list duration predictions was considered. However, a study by Wright *et al.* [15] compared the predictive accuracy on operating list duration of a model using only average durations of past operations with a regression model that included a number of patient and clinician factors known to affect surgical duration. This study found no significant difference in the predictive accuracy between the two models. [15] For the purposes of this study, it was decided that it would not be worth the significant investment in time to collect the additional data necessary to construct a regression model, considering that it is likely to offer no improvement in predictive accuracy over the model eventually used in this study.

The durations of each of the 120 operating lists were obtained by subtracting the actual starting time of the first procedure from the actual finishing time of the last procedure on each list. The allocated amount of time for operating lists at the regional Queensland hospital was 240 minutes. List durations equal to or longer than 260 minutes were classified as over-runs, and list durations that were equal to or shorter than 220 minutes were classified as under-runs. Those that were between 220 and 260 minutes were classified as on time. Although there is no widely accepted definition for on-time, over- and under-runs, the preliminary data collected for this project showed that a 20 minute margin was representative of the duration of some short surgical procedures, and thus would have some utility in demonstrating that over- and under-running lists could benefit from the omission or addition of a short procedure respectively.

Table 1. *Breakdown of lists without a cancellation, and the sensitivity and specificity of the model to predict which of these lists over-ran, under-ran, or ran on-time.*

	Operating lists without a cancellation (95% confidence intervals)		
Timing	As a percentage of all lists that did not have a cancellation	Sensitivity of prediction	Specificity of prediction
Over-run	45% (36-54%)	84% (65-94%)	82% (71-89%)
Under-run	37% (28-46%)	84% (62-94%)	85% (75-91%)
On-time	18% (11-25%)	73% (58-84%)	85% (73-93%)

The numbers of true on-time, over- and under-running lists were compared with the number of predicted on-time, over- and under-running lists to perform a sensitivity and specificity analysis.

Results

Twenty-eight percent (95% CI 19-37%) of the 120 operating lists suffered a cancellation, of which 79% (95% CI 75-83%) were predicted to over-run their scheduled duration. An analysis of all lists that did not suffer any cancellations is shown in Table 1. The sensitivities and specificities of the model to predict whether these lists over-ran, under-ran or ran on-time is also given. This gives an indication of the predictive power of the model – for example, a sensitivity of 84% for over-runs means 84% of lists predicted to over-run actually over-ran, and a specificity of 82% for over-runs means 82% of lists predicted not to over-run did not act actually over-run.

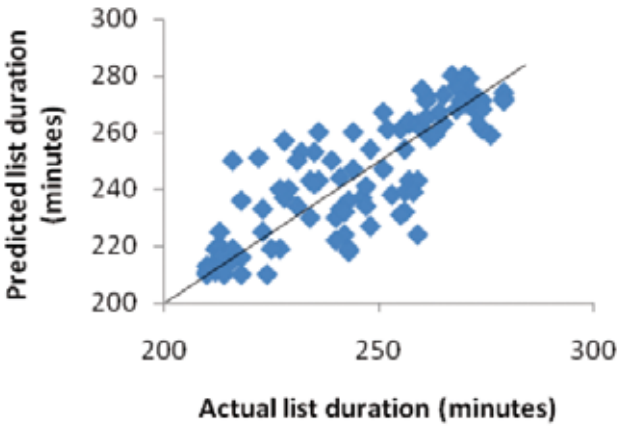

Figure 1. *Predicted duration of list plotted against actual duration of list (lists with cancellations are excluded). The diagonal line is the line of identity (predicted duration equals actual duration).*

This reasonably good ability of the computer estimates to predict operating list duration is shown graphically in Figure 1: the overall correlation coefficient, r is 0.83 ($r^2 = 0.68$; $p < 0.001$).

Tables 3 to 11 contain summary descriptive results for the types of procedures that were included in the 120 operating lists analysed in this study.

The procedures with the smallest coefficients of variation were haemorrhoidectomy (17%), excision of lesion of skin and subcutaneous tissue of foot (19%), incision of pilonidal sinus or cyst (10%), interruption of sapheno-femoral junction varicose veins (18%), hemithyroidectomy (17%), carpal tunnel release (18%), release of tendon sheath of hand (13%), total knee replacement (15%) and total hip replacement (17%).

The procedures with the largest coefficients of variation were arthroscopic repair of meniscus of knee (41%), closed reduction of fracture of distal radius with internal fixation (41%), decompression of subacromial space (37%), primary repair of nerve (39%), excision of lesion of skin and subcutaneous tissue of lip (44%), excision of lesion of skin and subcutaneous tissue of ear (42%).

Discussion

Data analysis

Consistent with expectations, more than one quarter (28%) of the operating lists in this study suffered a cancellation, and the vast majority of these (79%) were lists that were predicted by the model to over-run their scheduled time. This supports the notion that over-bookings leading to over-running operating lists are a significant cause of same-day surgery cancellations.

When the operating lists without cancellations were analysed, it was found that 45% over-ran and 37% under-ran their scheduled time. Only 18% of lists actually ran on-schedule. Although there is only limited published data on the prevalence of over- and under-running operating

Table 2. *Comparison of the prevalence of over-run, on-time and under-run operating lists.*

Timing	This study	Pandit *et al.* [1]	Widdison *et al.* [2]	Barr *et al.* [3]
Over-run	45%	53%	42%	21%
On-time	18%	10%	19%	47%
Under-run	37%	37%	39%	33%

lists in hospitals, the proportion of operating lists running off-schedule in this study can be compared to that of three United Kingdom (UK) hospitals as shown in Table 2. Side-by-side comparison shows that the regional Queensland hospital in this study had a greater proportion of over-runs and a lower proportion of on-time lists than all but the study by Pandit *et al.* [1] The proportions of under-runs were similar between all studies, which ranged from 33 to 39%. These findings show that over- and under-running of operating lists is at least as prevalent, if not more-so at the regional Queensland hospital in comparison to UK hospitals that have been previously studied.

Of the operating lists without cancellations that over- or under-ran scheduled time, the vast majority were prospectively predicted to over-run (84%) and under-run (84%), respectively. As the predictive calculations of the model in this project were based on the sum of estimated operation durations and their anaesthetic and turn-over times, these findings support the hypothesis that over-booking and under-booking are the main causes of operating lists running off-schedule, as opposed to other demonstrated causes of prolonged or shortened surgical duration (such as patient factors, surgical techniques, or skills of the anaesthetist or surgeon) affecting surgical duration that the model would not have accounted for. [12-14]

If booking errors occur because the people booking the operating lists do not know (or falsely believe that they know) the duration of the individual operations on those lists, a strategy that could be used to reduce these booking errors would be to use the similar methods of data collection employed in this study. Data about the average durations and variation in duration of all of the operations that a surgical team has performed in the past year can be presented to surgical teams to assist them in scheduling their operating lists. One study has shown that surgical teams that use predicted durations to schedule cases have fewer under-runs, over-runs and cancellations than teams that did not use predicted durations to schedule cases. [16]

It is important to recognise that booking errors may not be 'errors' at all, and that operating lists may be intentionally over- or under-booked. The possibility of intentional over- and under-bookings was raised by the findings of one study that showed surgeons who over-booked operating lists had very accurate estimates of the duration of individual operations (inclusive of anaesthetic durations) on their operating lists. [1] It has been suggested that lists may be intentionally over-booked in the face of pressures to reduce surgical waiting lists or meet hospital budgets. One study indicated that some surgeons over-book lists because there is a perception from their colleagues that booking fewer cases means they are 'not working hard'. [17] It has been suggested that lists may be intentionally under-booked for teaching purposes, low bed availabilities for post-operative care or to accommodate planned staff absences for meetings and other activities. [1,2] It is important to investigate in a follow-up study whether or not intentional over- and under-booking occurs, and if so, the reasons behind why it occurs must be identified as strategies may need to be tailored to address the specific underlying cause.

Other uses of surgical duration data

Data on durations of surgical procedures can be useful for costing services for the purposes of Medicare rebates. If the Medicare rebate for a given procedure is to reflect the cost of delivering the procedure, then procedure duration must be taken into account as it has been shown in many studies that staff hourly wages represent the greatest proportion of hospital costs. [10,18,19]

The collection of surgical duration data could be useful in allowing surgical teams to compare the present rate at which they complete their procedures with past performances. Analysis of these trends could help clinicians to identify patterns of change in their performances and identify the relationship of this to other key factors (such as changes in staff, use of equipment, surgical technique or patient load) so that changes can be made and clinical and economic outcomes improved.

Limitations

This study was performed in a regional hospital in Queensland, Australia. As a regional hospital, the scope of the operations performed at the hospital are narrower than that provided at a major metropolitan centre. Intuitively, with a narrower scope of operations, surgeons at a regional centre would be more accurate at estimating the duration of their operating lists compared with their metropolitan counterparts. The implications mean that generalisations based on the results in this study to a non-regional hospital may be limited. In addition, it should be noted that hospitals outside of Queensland may follow different protocols with respect to operating list scheduling (for example, in some hospitals the surgeon is not solely responsible for planning each operating list).

At the regional Queensland hospital in this study, only 240 minute (half-day) operating lists are used. This differs from some other hospitals, where 480 minute (full-day) operating lists are also utilised. According to the theatre administration, this is due to the limited number of operating rooms at the hospital and the need to accommodate the operating lists of all surgeons. The implication of not being able to analyse full-day lists in this study is that the differences in over- and under-running between half and full-day lists cannot be explored. This could be an area of interest for a follow-up study, as it is plausible that the surgeons may find it easier to estimate the duration of their half-day lists compared to longer full-day lists when scheduling their operations. [1]

At the hospital in this study, the start and finish time for each operation (from which the mean durations of operations are derived) are entered into the ORMIS computer system by a theatre staff member at the conclusion of each operation. Errors may have occurred where clock times are misread, finish times are estimated (i.e. the staff member enters the times into the computer before the operation is finished), or the data is entered incorrectly or not entered at all. However, errors of this kind were probably small in this study as a large database was used, where all data was checked to remove any obviously invalid entries such as those containing missing data, negative operation durations and impossibly short or long operation durations.

Conclusion

This study has shown that over- and under-booking are the most likely cause of operating lists running off-schedule. It is important to be aware that although over- and under-booking may not be the only causes of operating lists running off-schedule, they are significant and modifiable factors that if addressed correctly, could improve outcomes for patients (by reducing cancellations), doctors (by utilising their time more efficiently), and the health system (by reducing costs).

It is hoped that this study will be the catalyst for further research investigating the aetiology of booking errors, so that practical steps can be taken to avoid booking errors and minimise the negative consequences associated with them.

Conflicts of interest

None declared.

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Table 3. *Orthopaedic hand operations.*

	Carpal tunnel release (unilateral)	Palmar fasciectomy for Dupuytren's contracture involving 1 digit	Release of interphalangeal joint capsule for Dupuytren's contracture	Release of tendon sheath of hand	Open reduction of fracture of distal phalanx of hand with internal fixation
Mean duration in minutes	47	70	56	47	94.6
Median duration minutes	45	70	49	46	94
Standard deviation	8.4	22.7	19.9	6.3	25.4
Coefficient of variation	0.18	0.32	0.35	0.13	0.27
Sample size	181	14	6	5	7

Table 4*. Orthopaedic arm and shoulder operations.*

	Decompression of subacromial space	Closed reduction of fracture of distal radius	Closed reduction of fracture of distal radius with internal fixation	Repair of rotator cuff	Repair of rotator cuff with decompression of subacromial space
Mean duration in minutes	85	51	63	93	87
Median duration minutes	47	19	26	70	59
Standard deviation	31.3	10.7	25.9	24.2	20.5
Coefficient of variation	0.37	0.21	0.41	0.26	0.24
Sample size	5	53	17	14	20

Table 5. *Arthroscopic knee procedures.*

	Arthroscopy of knee	Arthroscopic debridement of knee	Arthroscopic meniscectomy of knee	Arthroscopic meniscectomy of knee with debridement, osteoplasty or chondroplasty	Arthroscopic repair of meniscus of knee	Arthroscopic reconstruction of cruciate ligament of knee with repair of meniscus
Mean duration in minutes	62.4	63.8	57.8	60.5	64.5	113.4
Median duration minutes	60	57.5	58	61	57.5	112
Standard deviation	17.1	19.0	12.6	12.8	26.6	34.2
Coefficient of variation	0.27	0.30	0.22	0.21	0.41	0.30
Sample size	132	20	16	14	6	13

Table 6. *Joint replacements, ankle procedures, and primary repair of nerve.*

	Total knee replacement	Total hip replacement	Revision of total arthroplasty of hip	Open reduction of dislocation of ankle with internal fixation	Open reduction of fracture of ankle	Open reduction of fracture of ankle with internal fixation of diastasis, fibula or malleolus	Primary Repair of nerve
Mean duration in minutes	123.4	113.5	169.8	97.2	102.8	103.2	70.0
Median duration minutes	122.5	116	172.5	106.5	105	102	65
Standard deviation	18.5	19.2	55.9	29.4	25.7	30.8	27.0
Coefficient of variation	0.15	0.17	0.33	0.30	0.25	0.30	0.39
Sample size	174	74	12	10	9	78	19

Table 7. *General surgery of hernias.*

	Laparoscopic repair of inguinal hernia, unilateral	Open repair of inguinal hernia, unilateral	Repair of umbilical hernia	Repair of incisional hernia	Repair of incisional hernia with prosthesis
Mean duration in minutes	89.4	80.7	69.4	101.1	125.3
Median duration minutes	90	78	68	94	122
Standard deviation	22.7	20.5	17.4	36.8	27.9
Coefficient of variation	0.25	0.25	0.25	0.36	0.22
Sample size	25	103	76	24	7

Table 8. *Appendicectomies and cholecystectomies.*

	Open appendicectomy	Laparoscopic appendicectomy	Laparoscopic cholecystectomy	Laparoscopic cholecystectomy proceeding to open cholecystectomy	Open cholecystectomy
Mean duration in minutes	79.4	94.6	103.1	116.8	111.7
Median duration minutes	76	90	99.5	117	101
Standard deviation	28.9	23.9	27.7	34.1	41.3
Coefficient of variation	0.36	0.25	0.27	0.29	0.37
Sample size	36	213	264	9	23

Table 9. *General surgery of breasts, thyroids, and varicose veins.*

	Mastectomy (including axillary node dissection)	Excision of lesion of breast	Total thyroidectomy	Hemithyroidectomy	Interruption of sapheno-femoral junction varicose veins
Mean duration in minutes	116.6	76.6	166.4	114.5	90.8
Median duration minutes	115	73	147	116	92.5
Standard deviation	24.0	25.3	57.4	20.0	16.4
Coefficient of variation	0.21	0.33	0.35	0.17	0.18
Sample size	39	75	26	23	10

Table 10. *Anterior resections, haemorrhoidectomies, and pilonidal sinus surgery.*

	Anterior resection	Haemorrhoidectomy	Excision of pilonidal sinus or cyst	Incision of pilonidal sinus or cyst
Mean duration in minutes	248.8	57.6	63.4	46.9
Median duration minutes	282	59	62	47
Standard deviation	62.6	9.5	14.1	4.6
Coefficient of variation	0.25	0.17	0.22	0.10
Sample size	5	17	15	19

Table 11. *Excision of lesion of skin and subcutaneous tissue.*

	Ear	Eyelid	Foot	Hand	Leg	Lip	Neck	Nose
Mean duration in minutes	70.9	60.5	51.8	64.4	57.2	63.9	65.3	72.6
Median duration minutes	66	58	52.5	56.5	56	52	62	71
Standard deviation	29.6	18.2	9.6	23.4	13.9	28.0	19.6	25.0
Coefficient of variation	0.42	0.30	0.19	0.36	0.24	0.44	0.30	0.34
Sample size	27	6	8	8	33	17	23	58

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Investigation of lactate dehydrogenase isoenzymes as candidate biomarkers of idiopathic pulmonary arterial hypertension

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This study investigates the activity and expression of lactate dehydrogenase (LDH) in idiopathic pulmonary arterial hypertension (IPAH) patients. IPAH is a rare and highly fatal disease with a median life expectancy at diagnosis of only 2.8 years. Ideally a simple blood test for biomarkers could simplify the physician's diagnostic work-up, resulting in earlier diagnosis and successful institution of therapy. Recent publications suggest IPAH may behave like cancer, with monoclonal proliferation and a shared pathway of mitochondrial dysfunction. LDH is often upregulated in cancers, and a similar elevation is suspected in IPAH. Discovering similar patterns of flux in the cellular bioenergetics of IPAH and cancer would support the emerging theory that IPAH has a 'cancer phenotype'. Quantitative proteomic analysis of fourteen lung tissue homogenate samples (seven lobectomy, seven IPAH) was performed using liquid chromatography – tandem mass spectrometry (LC-MS/MS). The lung samples, as well as 30 plasma samples (ten normal, 20 IPAH) were analysed for LDH fractional isoenzyme activity and expression. A pyruvate-to-lactate spectrophotometric activity assay was performed on the 44 samples, followed by LDH isoenzyme separation on thin-layer agarose gel and densitometric analysis. A significant link exists between IPAH and increased plasma and lung levels of LDH-1 ($P = 0.0114$ and 0.0262 respectively on Mann-Whitney U test). Receiver Operating Characteristic analysis demonstrated plasma LDH-1 had biomarker sensitivity and specificity of 80%. Measuring plasma LDH-1 appears clinically useful in diagnosing IPAH. This work supports the re-evaluation of IPAH as a cancer-like disease and suggests a new biomarker.

Introduction

Idiopathic pulmonary arterial hypertension (IPAH), first characterized in 1951, is pulmonary arterial hypertension (PAH) of unknown aetiology. [1] Clinically, it is defined by elevated mean pulmonary arterial pressure (mPAP) ≥25mmHg at rest or ≥30mmHg in exercise, and normal pulmonary capillary wedge pressure (PCWP) of ≤15mmHg. [2] Although rare (1-2 cases per million), IPAH is devastating. [3] It is 2.3 times more common in females and characteristically strikes during reproductive years. [4] In the natural history of the disease, patients suffer extremely poor quality of life and a high mortality rate comparable to many cancers, with life expectancy only 2.8 years at diagnosis. [5]

IPAH is notoriously difficult to diagnose. Not only is it extremely rare, but it also occurs in people with none of the classic risk factors for pulmonary arterial hypertension (i.e. connective tissue disease or HIV). [6] The typical IPAH patient is an otherwise healthy female aged in her thirties presenting with very non-specific symptoms, usually 'shortness of breath.' Other common presentations include fatigue, weakness, angina, syncope, peripheral oedema and abdominal distension. [7] Due to these barriers to diagnosis, median time from presentation to diagnosis is two to three years. [8] By then, 80% of patients have deteriorated to NYHA functional class III or IV. [9]

The current gold standard for IPAH diagnosis is right heart

catheterisation (RHC). Although informative, RHC is expensive and also highly invasive, raising particular risks for the haemodynamically fragile IPAH patient. Ideally a simple blood test for biomarkers could simplify the physician's diagnostic work-up, resulting in earlier diagnosis and successful institution of therapy. While several IPAH markers have been suggested, none have yet made it to the clinical setting. [10,31]

IPAH : A cancer-like disease?

Recent re-appraisals of IPAH suggest it may be a cancer-like process in aetiology, pathology and therapeutic response. [14] While IPAH was first explained as a disease of unexplained increase in pulmonary arterial tone, it was then discovered that extreme vasoconstriction occurs only in the minority of patients. Scientific investigation next identified that IPAH was histopathologically defined by proliferation of pulmonary artery endothelial cells (PAECs) and pulmonary artery smooth muscle cells (PASMCs). Recently, this proliferation was found to be strictly monoclonal, whereas the vascular hypertrophy of secondary PAH is mixed-form. [32]

The scientific literature supports this reinterpretation of IPAH as a 'neoplasia of the pulmonary circulation.' [15] The BmprII mutation causing familial pulmonary arterial hypertension (fPAH) also causes colon cancer. [33] Survivin, an anti-apoptotic molecule upregulated in most cancers, is linked to pulmonary vascular remodelling. [34] Further, offering promise for new clinical therapies, chemotherapy can increase survival in IPAH by up to 25%. [35]

Most compellingly, a pathway common to both cancer and IPAH has now been identified. Otto Warburg proposed in 1924 that altered glucose metabolism was central to the origin and maintenance of cancers. [36] Whereas normal cells increase their rate of glycolysis only when triggered by hypoxia, cancer cells have increased glycolysis even in a normoxic environment due to their defective mitochondria. The 'Warburg phenotype' is characterised by mitochondrial hyperpolarization, and downregulation of pyruvate dehydrogenase activity and hydrogen peroxide (H_2O_2) production. [37] It is this concept of 'inappropriate glycolysis' which underpins innovative technologies such as fluorodeoxyglucose positron emission tomography (FDG-PET).

Both IPAH and cancerous cells share this Warburg phenotype due to their mitochondrial dysfunction, which disrupts the mitochondria-ROS-HIF-1a-Kv1.5 O_2-sensing pathway. When the mitochondria become

dysfunctional, pyruvate dehydrogenase kinase (PDK) is activated. PDK phosphorylates and inhibits pyruvate dehydrogenase, such that most cellular pyruvate is metabolised by LDH into lactate. In the cytosol, this increases the rates of glycolysis and LDH activity. [15] In the mitochondria, decreased anaerobic respiration results in decreased production of reactive oxygen species such as hydrogen peroxide, triggering the activation of hypoxia-inducible-factor 1a (HIF-1a). By this stage, the mitochondria have become hyperpolarized, dysmorphic and anti-apoptotic. [38,39]

HIF-1a downregulates voltage-gated potassium channels such as Kv1.5, disrupting the body's oxygen-sensing system and worsening lung function. Reduced Kv1.5 also causes cell membrane depolarization, resulting in the cell flooding with cations (Ca2+ and K+). Increased intracellular Ca2+ causes vasoconstriction and activation of nuclear factor activating transcription (NFAT), promoting cellular proliferation. Increased intracellular K+ represses caspase activity, to decrease the rate of apoptosis. Consequently, in both IPAH PASMCs and cancer cells this dysfunctional pathway creates a pro-proliferative, apoptosis-resistant cell line. [40]

Proteomic analysis of IPAH samples was conducted to determine if any proteins associated with cancer were also upregulated in IPAH. Investigation of this putative 'cancer-like behaviour' may generate a double benefit, adding further data to the literature on IPAH's pathogenesis, as well as lighting the way to new diagnostic biomarkers.

In this study, proteomic work suggested LDH H was increased in IPAH lung samples. Lactate dehydrogenase (LDH) is a cytoplasmic enzyme catalysing the final step of anaerobic glycolysis. [37] The two major subunits of LDH are labelled M (coded for by the LDHA gene) and H (coded for by the LDHB gene). They assemble randomly to form 5 tetrameric isoenzymes: LDH-1 (H4), LDH-2 (H3M1), LDH-3 (H2M2), LDH-4 (H1M3), and LDH-5 (M4). The observed increase in LDH H was evaluated using an independently-performed assay and isoenzyme electrophoresis, with assessment of diagnostic utility in lung and plasma samples.

Methods

Lung Samples

Fourteen lung tissue homogenates used from Lobectomy (n=7) and IPAH (n=7) donors (Table 1). Lobectomy samples were healthy lung sections from lung cancer patients undergoing surgery. IPAH samples were hypertensive lung sections from transplant. One gram of lung tissue was immersed in 15mL 0.1M phosphate buffer (pH 7.4) with 1mM EDTA and 1mM DTT (dithiothreitol), and homogenised on ice with a PT-K Polytron® Stand Homogenizer (Kinematica AG, Switzerland).

Plasma Samples

Thirty plasma samples used from Control (n=10) and IPAH (n=20), matched for mean age and sex as far as was possible. Controls were healthy and medication-free. IPAH samples were obtained at the time of diagnosis, when patients were naïve to IPAH therapy.

Table 1. *Demographics of the 44 subjects (14 lung tissue and 30 plasma samples).*

	'Control' Group Plasma Samples (n=10)	'IPAH' Group Plasma Samples (n=20)	'Lobectomy' Group Lung Samples (n=7)	'IPAH' Group Lung Samples (n=7)
Gender Distribution	9 female 1 male	17 females 3 males	4 females 3 males	5 females 2 males
Mean Age	31.6 y.o.	46.8 y.o.	66.6 y.o.	39.1 y.o.
Age Range	22-57	29-68	50-79	28-51

1. Proteomics: Label-free LC-MS/MS

Lung samples in lithium dodecyl-sulfate (LDS) buffer underwent electrophoresis on bis-tris sodium dodecyl-sulfate (SDS) gels, then were destained with ammonium bicarbonate in acetonitrile (ACN) and digested with trypsin. Peptides extracted in formic acid/ACN were loaded on the LC-MS/MS. The program DeCyder MS identified and sequenced peptides based on ion intensity, LC retention time and m/z (molecular weight/charge) ratio, with inclusion cut-off 3-peptide validation. Amino acid structure was entered into Turbo SEQUEST search engine and compared against RefSeq human peptide sequence database.

2. Total LDH activity assay

The reagents for this stage were:

- 0.1M potassium phosphate buffer (PPB) (BDH Laboratory Supplies, Poole UK) at pH 7.4 and 30°C.
- NADH : 3.1 mM NADH (Sigma-Aldrich Company Ltd, Dorset UK) in PPB.
- Pyruvate in buffer: 11 mM pyruvate (Sigma-Aldrich Company Ltd, Dorset UK) in PPB.
- Sample (plasma, lung tissue): 10µL sample, 40µL PPB vortexed and on ice. Spectrophotometer: UV spectrophotometer (Hitachi U-3000) at 340nm, with 'UV Solution 2.0' software, and cuvette at 30°C.

440µL PPB, 30µL NADH solution, 10µL of diluted sample in cuvette. 30µL pyruvate solution added and solution inverted. Total LDH activity calculated through LDH-catalysed conversion of pyruvate to lactate, following decrease in NADH. Decreased absorbance recorded over 3 minutes, then Beer-Lambert's Law ($A\lambda = \varepsilon cL$) applied to determine sample activity. [41,42]

3. Separation of lactate dehydrogenase isoenzymes

The reagents for this stage were:

- Electrophoresis Buffer: 10.3g sodium diethylbarbiturate (Sigma-Aldrich Company Ltd, Dorset UK), 0.35g ethylenediaminetetraacetic acid (EDTA, BDH Laboratory Supplies, Poole UK), 7mL 1M HCl (BDH Laboratory Supplies, Poole UK) in dH2O, with pH 8.6 at 20°C, made up to 1.0L.
- Gel Buffer: 1.34g sodium diethylbarbiturate, 0.035g EDTA and 5g sucrose in dH2O, with pH 8.6 at 20°C, made up to 100mL.
- L+-lithium lactate solution: 2.4g L(+)-lithium lactate (Sigma-Aldrich Company Ltd, Dorset UK) in 50mL dH2O, pH 7.0 at 20°C.
- PMS incubating solution: 1mL 200mg/L phenazine methosulfate (PMS) (Sigma-Aldrich Company Ltd, Dorset UK) ; made up immediately prior to use in dark.
- β-NAD / lactate solution: 3mg β-nicotinamide adenine dinucleotide (β-NAD) (Sigma-Aldrich Company Ltd, Dorset UK), 7.2mg tetranitroblue tetrazolium (TNBT) (Fluka Biochemika, Switzerland) in 0.9mL L+-lithium lactate solution and 2.1mL dH2O.
- Samples (plasma or lung homogenate): based on total LDH activity measurements, samples were diluted with phosphate-buffered saline (PBS, Sigma-Aldrich Company Ltd., Dorset UK) to aliquots with constant total LDH activity. *:*

1% agarose/gel buffer solution poured into 0.75mm thin-layer gel, with 2µL of sample in each well. Gel run at 200V, 40mA for 1 hour 45 minutes on Pharmacia Fine Chemicals Flat Bed Apparatus FBE-3000, then incubated 30 minutes at 37°C in 1mL PMS solution, 3mL β-NAD/ lactate solution, 7mL dH2O, with isoenzymes reacting as follows: [43-46]

$$\text{Lactate} + NAD^+ \leftrightarrow \text{Pyruvate} + NADH + H^+$$

$$NADH + PMS \leftrightarrow NAD^+ + PMS\text{-}H$$

$$PMS\text{-}H + TNBT \leftrightarrow PMS + TNBT\text{-}Formazan$$

Gel was scanned on Kodak 440 Image Station Densitometer (Kodak,

USA), and intensity profile exported to The Scientific Figure Processor 6.0 program (Biosoft, UK). Each isoenzyme's area under the curve (AUC) as fraction of sample total plotted in GraphPad Prism 4.0 for Windows (GraphPad Software, Inc., USA).

4. Calculation of LDH subunit levels

To interpret relative LDH subunit expression, calculations were applied to data from total LDH activity assays and isoenzyme electrophoresis. For example, to determine relative proportion of LDH H, 'XLDHH % = 100 (ΣLDHH subunits) / (total LDH mean activity)'. The other LDH subunit's expression was then simply 'XLDHM % = 100 – XLDHH %'. Individual values were obtained for each sample, then group mean values calculated.

5. ROC analysis to determine sensitivity and specificity

Parameters showing significant changes were analysed in Receiver Operating Characteristic (ROC) curves in GraphPad Prism 4.0 for Windows with 95% confidence intervals.

Results

1. Proteomics

Seventy-three proteins were differentially expressed between IPAH and control groups; Table 2 presents data for LDH subunits. LDH H subunit was expressed 2.7-fold higher in IPAH compared to controls, and this change was statistically significant (P = 0.02).

Table 2. *Data obtained from proteomic analysis (liquid chromatography – tandem mass spectrometry) of fourteen lung tissue samples. Seventy-three proteins were differentially expressed between IPAH and control groups; lactate dehydrogenase was selected for further investigation, and data relating to its subunits is presented here. SD = standard deviation.*

Protein	Number of Peptides	Lobectomy Mean ion intensity ± SD	IPAH Mean ion intensity ± SD	Fold difference	P value (Mann-Whitney U test)
LDH H subunit	3	58.7 ± 27.1	163.9 ± 47.8	2.7	0.02
LDH M subunit	4	88.6 ± 44.4	137.9 ± 109.0	1.6	0.73

2. Total LDH activity assay

Lung Homogenate: Mean total LDH activity was 1.4-fold higher in 'IPAH' group (37 U/g) compared to 'Lobectomy' (26 U/g) (Figure 1A). However, on Mann-Whitney U test, this difference was non-significant (P > 0.05).

Plasma: Mean total LDH activity was only 1.15-fold higher in 'IPAH' group (310 U/L) compared to 'Control' (269 U/L) (Figure 1B); this difference was not significant (P > 0.05).

3. LDH isoenzymes

Lung Homogenate: Mann-Whitney U test showed both LDH-1 and LDH-2 were significantly upregulated in the 'IPAH' cohort (P=0.0262 and P=0.0379 respectively; Figure 1C).

Plasma: LDH-1 was increased by mean value 32 U/L (a 52% elevation in isoenzyme fraction), with proportional change significant on Mann-Whitney U test (P=0.0114). LDH-5 was significantly downregulated in IPAH (P=0.0186) from mean value 8 U/L to 4 U/L. (Figure 1D).

4. LDH H subunits

Lung Homogenate: Mann-Whitney U test showed the proportion of LDH H subunit was significantly increased in the 'IPAH' group (61.5%) compared to the 'Lobectomy' group (52.7%), with P = 0.0111 (Figure 1E). Data for LDH H and LDH M was also compared with respective levels determined using proteomics. In both cases, there was good correlation between levels determined by proteomics and levels determined using enzyme activity and electrophoretic separation (Figure 2).

Plasma: Mann-Whitney U test showed proportion of LDH H subunit activity was highly significantly increased in the 'IPAH' group (72.9%) compared to the 'Control' group (67.8%), with P = 0.0030 (Figure 1F).

5. Sensitivity and specificity of LDH measurements

Lung Homogenate: LDH H subunit proportion was the best marker,

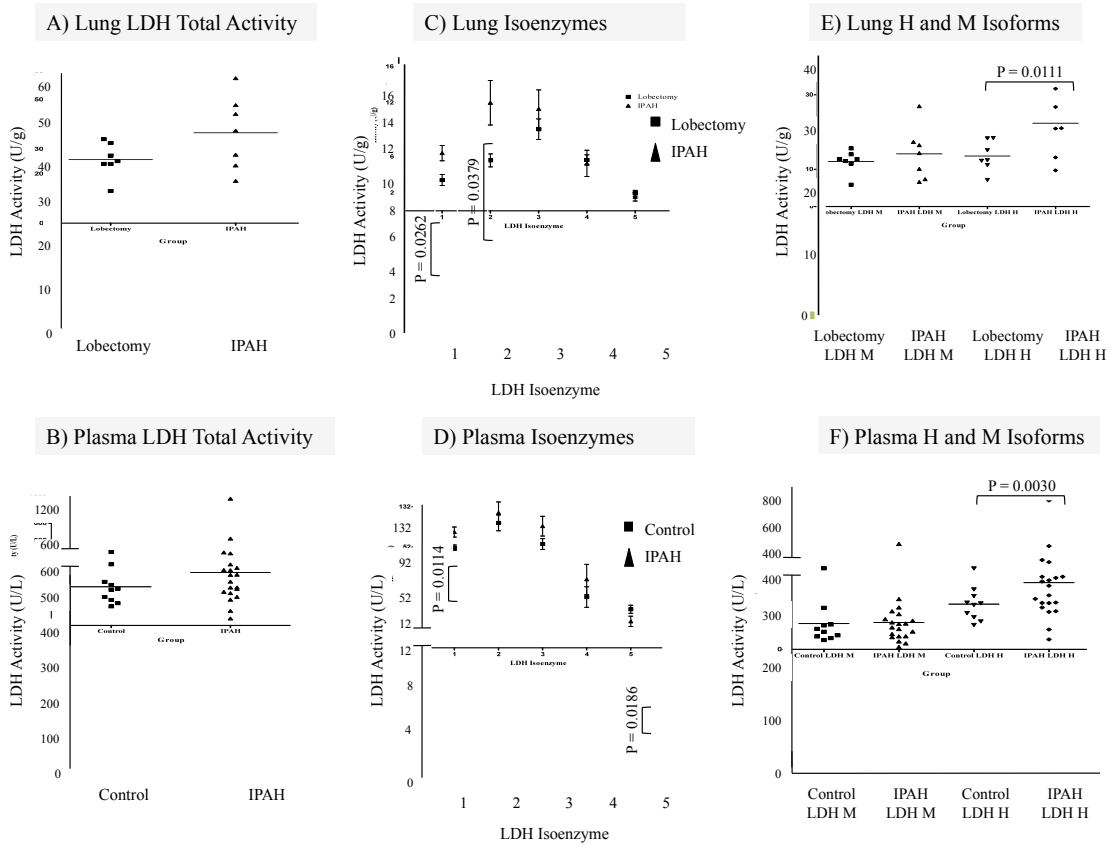

Figure 1. *Results of Total Activity Assay, Electroporesis and Isoform Quantification.*

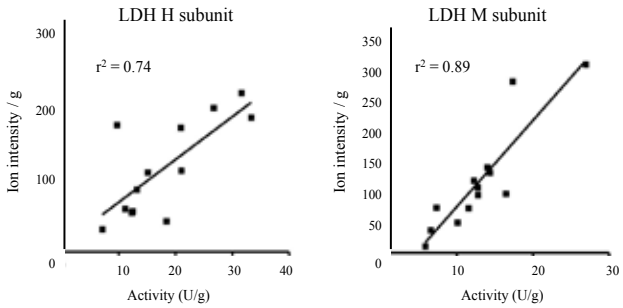

Figure 2. *Correlation of LDH isoform activity values from proteomics work with results from activity assay and electrophoretic separation.*

Table 3. *Receiver-Operating Characteristic values for lactate dehydrogenase parameters found to be differentially expressed between IPAH and control groups in lung tissue or plasma. In lung tissue, measuring proportion of LDH H subunit offers best discriminative value; in plasma samples, measuring LDH-1 activity is the best diagnostic marker. AUC = area under curve.*

	Enzymes	Cut-off for IPAH Diagnosis	Sensitivity	Specificity	AUC
Lung	LDH-1	≥ 4 U/g	86%	71%	0.86
	LDH-2	≥ 5 U/g	86%	71%	0.84
	LDH H subunit	*≥ 56%*	*86%*	*86%*	*0.90*
Plasma	*LDH-1*	*≥ 59 U/L*	*80%*	*80%*	*0.73*
	LDH H subunit	≥ 72%	50%	80%	0.58

with sensitivity of 86%, specificity of 86% and AUC of 0.90 at cut-off of 56% (Table 3).

Plasma: LDH-1 levels were the best discriminator for diagnosing IPAH, with sensitivity of 80%, specificity of 80% and AUC of 0.73 at cut-off of 59 U/L.

Discussion

From proteomic analysis of lung tissue from IPAH patients and control donors, an increase in LDH H levels in IPAH was observed. This finding was confirmed by measurement of LDH H activity, using electrophoresis to separate and quantify the LDH isoenzymes. In addition, LDH H levels were measured in plasma from IPAH patients and compared against healthy controls. Again, LDH H levels were found to be elevated.

It is possible that lung LDH H levels could be used as an IPAH marker. Indeed, in this study lung LDH H was the best-performing diagnostic biomarker with a sensitivity and specificity of 86%. However, in terms of invasiveness, performing lung biopsy is not an acceptable improvement on cardiac catheterisation. Thus, plasma LDH H (LDH-1) would be the preferable biomarker, with a sensitivity and specificity of 80% and requiring only venepuncture for sample collection.

Changes in LDH isoenzyme profile are already widely recognised as biomarkers in cancer and lung pathology. In cancer, LDH isoenzyme pattern can reflect underlying histology. Increased LDH-5 expression characterises many solid tumours, particularly carcinomas of the genitalia or digestive tract. In germ cell tumours however, there is a shift toward LDH-1 expression. [47-49] LDH activity can also differentially diagnose solitary pulmonary nodules as benign or malignant. [50]

Many lung pathologies also alter the isoenzyme profile. LDH-3 is most commonly affected, particularly when large numbers of alveolar macrophages are destroyed. [51] It is elevated in tuberculosis, pneumoconiosis, pulmonary alveolar proteinosis, pulmonary embolism, bacterial pneumonia and acute pulmonary oedema. [52-57] However, other patterns have also been found in pulmonary pathology. LDH-1 is elevated in both small-cell lung cancer and severe acute respiratory syndrome (SARS). It is sufficiently specific and sensitive to be a useful supporting biomarker in diagnosing SARS. [58,59] LDH-4 and LDH-5 increase in non-small-cell lung cancer (NSCLC) and transplant-related acute lung injury. [55] LDH-5 levels characteristically increase in pulmonary diseases where large numbers of neutrophils are undergoing apoptosis. [51]

Recent advances in elucidating the true pathogenesis of IPAH have paved the way for exploiting insights from foreign areas of medical research. There is now the exciting possibility of drawing upon decades of intense studies on cancer in order to rapidly improve outcomes in IPAH. Our finding that LDH H is upregulated in IPAH is consistent with PASMCs and PAECs exhibiting the 'Warburg phenotype.' It is possible that the increased LDH H levels are occurring as a result of cellular phenotypic shift to a state of increased glycolysis.

In this study, the LDH H increase was observed in lung tissue (a local sample) and corroborated in plasma samples - a logical finding given that the majority of the circulation passes through the lungs. The specific elevation in LDH H subunit fits well with the traditional paradigm that LDH H-dominant tetramers are usually of cardiovascular origin, while kidneys and liver mainly produce LDH-4 and LDH-5, the tetramers with high LDH M levels.

Genetic analysis would be useful to capture mutational or epigenetic changes to the LDHB gene underlying the increased expression of LDH H subunit. Immunohistochemical studies would also be desirable, as by identifying cells expressing LDH isoenzymes they could further expose the underlying disease process.

Greater evaluation of the glycolytic and mitochondrial pathways in IPAH is also required, since LDH is just one of many glycolytic proteins. Of note, the 73 proteins identified here did not include any of the other classic glycolytic proteins. However, other studies have validated components of the mitochondrial pathway, such as the Kv1.5 channel, in IPAH. [60]

Future studies should ideally enrol a greater number of subjects than the 44 studied here. While these results are promising, data is needed on the performance of LDH-1 in diagnosing IPAH with high sensitivity and specificity on a population level. It would also be logical in other follow-up studies to contrast the IPAH patients against other cardiorespiratory patients to ascertain the precise discriminatory powers of LDH-1 in a setting where baseline elevated LDH levels can be expected. Given the rarity of IPAH and consequent difficulty of enrolling subjects, these future directions may absorb many more years of research.

Conclusion

This is the first known investigation into LDH and its isoenzymes as candidate biomarkers for diagnosing IPAH. Investigations show that:

a) There is a significant increase in LDH H subunits in IPAH patients;

b) There is significant upregulation of LDH-1 and LDH-2 and downregulation of LDH-5; and

c) plasma levels of LDH-1 are the most accurate and clinically acceptable biomarker for diagnosing IPAH, with sensitivity and specificity both 80%.

This study supports the re-evaluation of IPAH as a cancer-like disease and suggests plasma LDH-1 (an LDH H homotetramer) may be useful in diagnosis.

Conflict of interest

None declared.

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A survey of the ophthalmic presentations and their outcomes to a general hospital Emergency Department over twelve months

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After graduation, Dr. Smith undertook further training in Emergency Medicine and related fields. He is a fellow of the college of Emergency Medicine and is a staff specialist Emergency Physician.

Aim: To survey the diagnoses and discharge status of the ophthalmic presentations to a general emergency department (ED). To compare the ED diagnosis with the ophthalmologist diagnosis of referred patients. **Methods:** A retrospective analysis of all the ophthalmic presentations to the Gosford District Hospital from 1 January 2005 to 31 December 2005 was carried out. All referrals to and admissions by ophthalmologists were reviewed for the final diagnosis. These outcomes were compared to the initial ED diagnosis. **Results:** There were 509 ophthalmic presentations to the ED in 2005: 51% had corneal trauma, 14% had an unspecified red or painful eye, 9% had an unspecified eye injury and 5% had blurred vision. Most patients were discharged without referral. Twenty-two percent of patients were referred to an ophthalmologist. Four percent were admitted and transferred to Sydney Eye Hospital. In those who were referred, 13% did not have records at the specified ophthalmologist, 24% were not recorded to which specialist they were referred and 26% had significantly different specialist opinion. **Conclusions:** More than half of ED ophthalmic presentations were for corneal trauma and only 22% of patients were referred to an ophthalmologist, while most were treated solely in the ED or referred to general practice. Potentially vision-threatening misdiagnoses included three cases of iritis, three of keratitis and two of retinal artery occlusion. ED diagnoses of corneal problems matched exactly with ophthalmic opinion. Interestingly, recording of the visual acuity occurred in only 27% of cases.

Background

Patients with acute ocular and visual problems present to various settings: the general practitioner (GP), the optometrist, the emergency department (ED) of the local hospital and other locations. In a review of the literature, it was observed that approximately one percent of ED presentations were for visual or ophthalmic problems. [1-4]

Previous studies have attempted to show the presentation load at general hospitals. Edwards [1] in 1987 made epidemiological conclusions based on an English hospital on data over fifteen years old, but without correlation between ED diagnosis and ophthalmologist diagnosis. Voon *et al.* [2] reviewed ocular trauma presentations in a Singaporean general hospital over a three month period in 1997, with emphasis on epidemiology of the mechanism of injury rather than outcome. Sanchez *et al.* [3] studied the presentations to a Spanish general hospital over nine months with regard only to the epidemiology of the patients presenting. Nash *et al.* [4] presented data from a national database in the USA from 1993 on the epidemiology of ocular presentations to general hospitals, but with no regard to the outcomes or accuracy of diagnosis. One Australian study regarding the epidemiology of ophthalmic presentations, by Kumar *et al.*, [5] was based on patients who were seen during the daytime at a dedicated eye hospital ED in 2001.

A recent Australian article reviewed only the referrals made from primary health providers to a dedicated ophthalmic emergency

service. [6] Over half the patients were referred from GPs. The article did not closely examine the referrals made from general ED doctors; rather it focused on the mistakes made by referring GPs. It found that iritis and viral conjunctivitis were commonly misdiagnosed by primary care providers and that antibiotics were routinely over-prescribed.

This is the first Australian study of ophthalmic presentations to a general ED. Numerous areas were examined including the frequency of diagnoses, the range of conditions diagnosed, discharge status of each presentation and the diagnosis made by the ophthalmologist if the patient was seen regarding their presenting problem. Several further factors were determined, including the most common diagnoses in patients presenting to a general ED with ophthalmic problems; and the correlation between the diagnosis made in the ED and that of the ophthalmologist.

Methods

Ethical approval for this study was gained through the Central Coast Area Health Service (CCAHS) Ethics Committee in September 2006. All presentation data were obtained by the Gosford ED Information Service from 1 January 2005 to 31 December 2005 inclusive. Using the International Classification of Disease system, patients presenting with ophthalmic or visual disturbance were included. All other presentations were excluded. Data were converted from the service's format to a Microsoft Access database and each patient's medical record was then retrieved by hand. The following data were then entered onto a standardised form: name, ED diagnosis, referral or admission outcome for that presentation, visual acuity (yes/no) and the name of the ophthalmologist to whom that patient was referred (if there was a referral).

In 41% of the presentations, no specific diagnosis was given by the ED doctor. Instead, a less specific symptom or finding was used. For the non-specific diagnoses by the ED, no mention of a differential diagnosis was made in the notes. Where a diagnosis was given, it was recorded as written by the ED doctor. There was only one data collector, who was not blinded to the study outcomes. All records of the patients referred to ophthalmologists were sought from the stated ophthalmologist (a total of five different area ophthalmologists). These were examined in each of the ophthalmic practices and the diagnoses added to the

standardised form. [7]

Seven patient records were unable to be obtained through the CCAHS as three patients' records were held at an offsite facility and four files were missing.

Results

There were 509 ED ophthalmic presentations to the Gosford ED between the dates 1 January 2005 and 31 December 2005 inclusive. Of these, 360 were males and 149 were females.

In only 27% of presentations was the visual acuity recorded (including the phrase "vision normal").

Table 1 shows the most common diagnoses made by the ED doctors. Diagnoses of fewer than two cases are not shown. The most common diagnoses made were for corneal trauma, such as abrasion, chemical splash or foreign body (316 presentations, 62%).

Table 1. *Commonest diagnoses made in ED for ophthalmic presentations, in absolute numbers.*

Diagnosis	Absolute patient number (%)
Corneal foreign body	184 (36)
"Red eye" (non-specific)	69 (14)
Corneal abrasion	52 (10)
"Trauma to eye" (non-specific)	48 (9)
"Blurred vision" (non-specific)	25 (5)
Chemical splash in eye	23 (5)
"Inflamed eye" (non-specific)	21 (5)
Migraine	10 (2)
"Itchy Eye" (non-specific)	6 (1)
Herpes Zoster ophthalmicus	4 (<1)
Fractured orbit	4 (<1)
Subconjunctival haemorrhage	3 (<1)
"Discharging eye"(non-specific)	3 (<1)
Stye	4 (<1)
Penetrating eye injury	2 (<1)
"Blindness one eye" (non-specific)	2 (<1)
Iritis	2 (<1)
Scleritis	2 (<1)
Total	*464 (91)*

Table 2 summarises the destinations for all the patients. Most patients were deemed well enough to be discharged as 'treatment complete,' or to be reviewed by the local GP or back at ED. Those transferred to Sydney Eye Hospital were for one case of endophthalmitis and three cases of penetrating eye globe injury.

One hundred and ten patients of the 509 were referred for ophthalmic opinion. In 26 of those 110, the patients' notes do not show to which specialist they were sent, simply "referred to ophthalmologist." A further fourteen patients of these 110 have no record of being seen at the ophthalmic practice to which they were referred.

The differing diagnoses between ophthalmologists and ED doctors are listed in Table 3. All 39 ED diagnoses of corneal pathology concurred with the ophthalmologist opinions (in traced records).

Discussion

Gosford ED is staffed by doctors in various stages of training. Most are post-graduate year one and two; that is, interns and residents. In this survey, the level of experience of the doctor was not recorded. It may be interesting in future studies to observe if note-keeping and accuracy

Table 2. *ED departure status of patients with ophthalmic presentations, in absolute numbers.*

Departure Status	Absolute patient number (%)
Discharged treatment complete	165 (32)
Discharged with referral to ophthalmologist	110 (22)
Discharged to GP	95 (19)
Discharged with review in ED	85 (17)
Uncertain outcome	17 (3)
Admitted under ophthalmologist	13 (3)
Patient record unavailable	7 (1)
Referred to maxillofacial surgeon	5 (1)
Admitted under ophthalmologist and transferred to Sydney Eye Hospital	4 (<1)
Admission under paediatrician	3 (<1)
Referred to neurologist	2 (<1)
Admission under ENT	1 (<1)
Admission under physician	1 (<1)
Patient left ED before attendance	1 (<1)
Total	*509*

Table 3. *Differing diagnoses between ED staff and ophthalmologists.*

Ophthalmologist Diagnoses (with number)	ED Diagnosis
Vitreous detachment (2)	
Chronic dacryocystitis (1)	
Cataract (2)	
Corneal foreign body (1)	
Lacrimal duct obstruction (1)	"Painful eye"
Conjunctivitis (2)	
Corneal abrasion (1)	
Herpes Zoster ophthalmicus (1)	
Keratitis (1)	
Iritis (3)	"Blurred vision"
Dendritic keratitis (2)	"Painful eye" (1) and Herpes Zoster
Retinal artery occlusion (2)	Blurred vision (1) and "blindness one eye"
Keratoconjunctivitis (1)	Iritis
Branch vein occlusion (1)	Migraine
Ischaemic optic neuropathy (2)	"Blindness one eye" (1) and migraine

of diagnosis differ between ED doctors of different clinical training.

Presentations to a general district hospital for ophthalmic problems were primarily for acute issues, corneal trauma accounting for the majority of cases. This is in keeping with observations made by Nash *et al.* [3] and Sanchez *et al.* [4]

A limitation of the study is that for all the presentations that were not referred to ophthalmologists, there was no way of checking accuracy of diagnosis. This should be addressed in future studies, preferably prospectively.

Conclusions

Superficial ophthalmic trauma is a very common ED presentation. For those patients referred to an ophthalmologist whose records can be traced, it appears that the majority were appropriately directed. The data shows that the ED doctors were more accurate in diagnosing corneal and eyelid problems than uveal, vitreous and retinal problems. Vision should be recorded in every patient who presents with visual or ocular symptoms. All referrals should be documented specifically and clearly.

Conflict of interest

None declared.

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Authors' Contributions

Rabin Bhandari collected the data and wrote the background, methods and results. Dr. Smith and Rabin Bhandari contributed equally to the discussion and conclusions.

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The Internet as a health information source for university students

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As the prevalence of those seeking health information online rises, the potential for information overload and misinformation increases. This study aims to evaluate and explore the Internet's role as a health information source, specifically for university students. In total, 120 university students were surveyed for their behaviours and attitudes when accessing online health information. Of the respondents, 61% had used the Internet as a personal health information source at least once in the past and 34% do so at least once a month. In comparison with other common information sources, the Internet was the third most commonly used (41%) behind General Practitioners (73%) and family and friends (60%). Despite this frequency of use, only 5% of participants regarded the Internet to be very accurate, while 27.5% had found health information on the Internet to be misleading. Online health advice had delayed appropriate medical treatment at least once for 28% of participants. Both information inaccuracy and treatment delay pose risks to health outcomes. The findings from this research provide a useful starting point for future research into Australian Internet health information seeking behaviour.

Introduction

Today, consumers have access to a diverse range of health information sources. Online health information seeking has been increasing amongst adults because the Internet offers convenient and abundant information. Twenty-seven percent of Australian Internet users seek health information online. [1-3] Accompanying this usage come the potential issues of information overload and misinformation. Other issues for consideration include complicating the doctor-patient relationship with inappropriate requests, delays in effective health treatment due to self-diagnosis, and misdiagnosis leading to adverse health outcomes. [4,5]

There are several key reports considering the quality of online health information, though most focus on the general population. [2,6,7] A study focusing primarily upon university students, a population subgroup for whom the Internet is an integral part of daily communication, has not previously been undertaken. [8,9]

Methods

The sample group for this study was Monash University students at the Clayton campus aged eighteen years and above. Approval for this project was obtained from the Monash University Standing Committee on Ethics in Research Involving Humans (SCERH).

A previously piloted survey designed by the authors was used to collect quantitative and qualitative data anonymously from university students on campus. Participants were selected at random and then invited to complete the self-administered survey. The key measures of interest were the frequency of student access to health information and the perceived reliability of online health information. Four different hypothetical health complaints (common cold, neck swelling, genital issues and depression) were used to study where and in which order health information would be potentially accessed for each scenario. Each health information source was ranked by number of people placing that source amongst the first three sources they would have accessed. The data was analysed using Microsoft® Excel 2003 and SPSS Graduate Pack Version 16.0 (SPSS, Inc., Chicago IL).

Results

One hundred and twenty-five surveys were distributed and 120 returned (response rate of 96.0%). The gender distribution was almost equivalent (52% male, 48% female), while 82% were aged 22 years or younger. In terms of faculty and course, medical students were the

highest represented (28%), followed by science students (17%) and engineering students (14%).

A General Practitioner (GP) was the most commonly used health information source (73%), closely followed by family and friends (60%), with the Internet being the third most accessed (41%) (Figure 1). Of the participants, 44.2% reported experiencing conflicting information in the past.

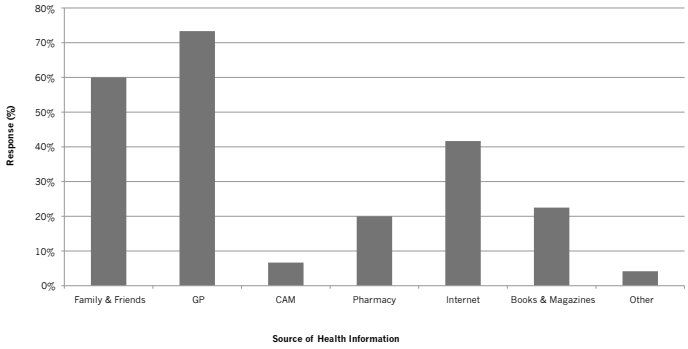

Figure 1. *Health information source used to access information (n=120).*

The use of the Internet as a health information source varied according to the type of hypothetical health problem presented (Table 1). For both the 'common cold' and 'neck swelling' the Internet was the fourth most popular health information source behind the GP, family and friends, and the pharmacy. However, for 'genital issues' the Internet was a more popular health information source, ranking second after the GP as the preferred information source. For 'depression' the Internet ranked third.

Of all participants, 73 (60.8%) had used the Internet as a personal health information source at least once, while 36 (30.0%) had looked up health information for others. The frequency of online health seeking was widely distributed, with 21 participants (52.6% of those who had searched online) doing so at least monthly. Google (www.google.com) was the most frequently used website.

When judging the quality of online health information, only 5.0% of participants deemed the Internet to be 'very accurate' (Figure 2). Of all participants, 27.5% had found health information on the Internet to be misleading. Twenty-eight point three percent of participants reported delaying appropriate medical treatment due to online health advice at least once, yet in most of the delayed cases, this had only occurred once or twice (85.5%).

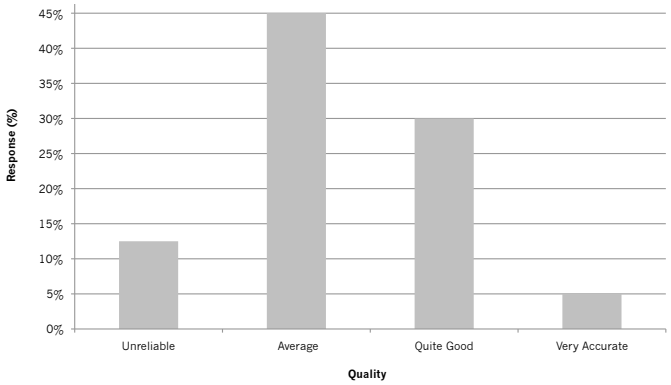

Figure 2. *Perceived quality of Internet health information by participants (n=120).*

Medical students were three times more likely to have found websites to be misleading than non-medical students (52.9% versus 17.4%, p=0.001). Most medical students (61.8%) rated the quality of health information to be 'quite good' compared to most non-medical students (55.8%) rating it as only 'average' quality.

Medical students searched for health information at much higher frequencies than their non-medical peers (p<0.001) (Figure 3). Table 2 shows that medical students were more likely to use a wider range of health information sites (such as the peer-reviewed eMedicine and Government health sites,) with non-medical students leaning towards general search engines (82.0% of non-medical respondents vs. 50.0% for medical respondents).

A total of 60.8% of participants agreed that the Government should provide better health information, with suggestions ranging from discussing mental health issues to creating more reliable Internet health sites. When asked about the best method of learning more about online health information, the two most popular choices were brochures (49.2%) and websites (50.0%).

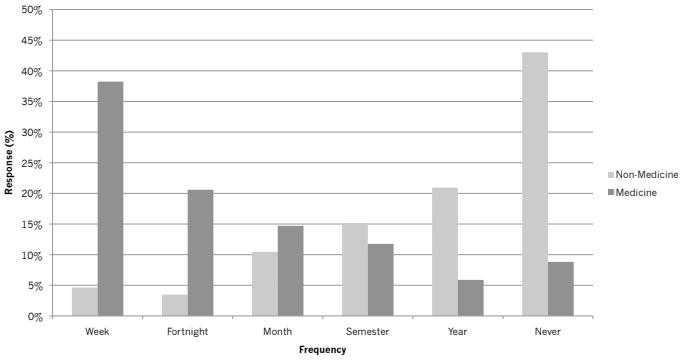

Figure 3. *Frequency of online health information seeking (n=116). Light grey = non-medical respondents, dark grey = medical respondents.*

Table 2. *Health websites accessed by respondents.*

Online resource	Medical students (n=26)	Non-medical students (n=28)
Google	12	17
General search engines	1	11
eMedicine	12	0
Library databases	5	3
Government-sponsored health sites	4	1
Other health sites	6	2
Percent respondents selecting more than one source	35%	18%

Table 1. *Health information source used for hypothetical health complaints.*

	Common Cold (n=120)		Neck Swelling (n=117)		Genital Issues (n=117)		Depression (n=117)	
Source	Rank	Score	Rank	Score	Rank	Score	Rank	Score
Family and friends	1	93	1	106	3	64	1	97
General Practitioner	2	89	2	85	1	103	2	74
Pharmacy	3	85	3	55	4	50	4	29
Internet	*4*	*25*	*4*	*37*	*2*	*65*	*3*	*55*
Complementary therapy	5	24	5	31	6	15	5	19
Books	6	11	6	13	5	29	5	19

Discussion

The results of this study demonstrate that the Internet is a commonly-used health information source for Monash University students and is utilised by a higher percentage when compared to the general public. [1] GPs and "family and friends" do however remain the most important sources, perhaps because they are considered to be more familiar and trustworthy. Despite this, the Internet was preferred over books and pharmacies in this study. Increasing familiarity with the Internet amongst university students, coupled with the convenience of accessing online information, could be the reason why these other traditional and perhaps more reliable sources are bypassed.

Conflicting health information was reported to be a common occurrence. In some ways, this may not be a negative finding as it may increase awareness that some advice may not always be accurate. However, this could create confusion in patients and result in self-misdiagnosis.

It is interesting to note that the preference of sources varies with respect to the perceived severity and social stigma attached to the condition being investigated. For genital issues, respondents indicated an inclination towards a more private and personal source such as the Internet, presumably because they may feel less embarrassed. Findings were similar for depression – another condition which potentially be socially-stigmatised. This is in contrast to 'everyday' conditions such as the common cold, where family advice is generally perceived as adequate.

The results showed a statistically significant difference between medical and non-medical students, where medical students searched for online health information at higher frequencies than their non-medical peers. It could be suggested that medical students, due to their education, were more capable of identifying a higher number of misleading sites. Perhaps finding these sites in the past, or hearing about them from their peers, has helped them utilise more reliable sources. They used both a wider range of searching techniques as well as more reputable sources. This trend towards better quality sites is reflected by most medical students rating the quality of online information as higher than non-medical students.

Limitations

Participants were asked to recall information regarding their past actions. This relied on long-term memory, subjecting the survey to recall bias. The study was also subject to selection bias as the small sample population comprised of a large number of medical students and may not reflect the general student population at Monash University.

Conclusion

The results illustrate that a significant number of university students use the Internet for health information, with varying search techniques and frequencies of usage. The Internet ranked higher in importance for health problems of a personal nature, and lower for common minor ailments. However, many were unsure about its reliability and a considerable number delayed appropriate treatment. The combination of uncertainty and treatment delay poses significant risks to health outcomes and is an issue worthy of intervention.

The findings provide some initial data for use in future research into online health-seeking by Australian university students.

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Use of retrograde intra-operative cholangiogram for detection and minimisation of common bile duct injury

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Lachlan submitted this article to the AMSJ while in his final year of medicine in 2009. During that year, he was awarded the Dr Elaine Katte Prize and the Australian Medical Association Memorial Prize.

Iatrogenic bile duct injury (BDI) is a known complication of laparoscopic cholecystectomy with serious consequences for the health of the patient. Intra-operative cholangiogram (IOC) has been shown to reduce the incidence of a major BDI, and is currently used routinely by the majority of surgeons in Queensland. This case report details the use of a 'retrograde IOC' for the detection of a BDI after inadvertent cannulation of the common bile duct (CBD). Application of this method has the potential to improve patient outcomes in two ways. Firstly, by limiting the degree of damage to the CBD, it may facilitate a simpler and more successful repair. Secondly, it provides a method of laparoscopic confirmation of BDI and, where laparoscopic hepaticojejunostomy is available, can entirely prevent the need for an open procedure.

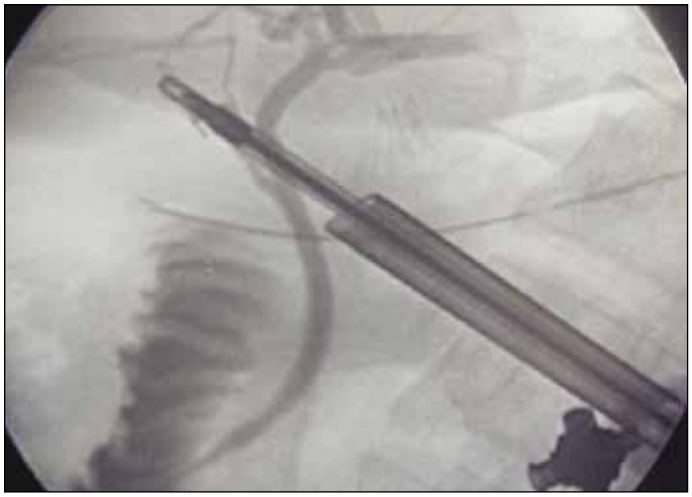
Introduction

Bile duct injury (BDI) remains one of the most feared complications of cholecystectomy, due to the potential for a significant impact on quality of life and increased mortality. [1] This complication is often of particular interest in relation to the laparoscopic approach, as some studies have shown the rates of BDI to be higher with laparoscopic procedures when compared to traditional open surgery. [2,3] One aspect of laparoscopic cholecystectomy and the development of BDI that has remained controversial for more than fifteen years is the routine use of intra-operative cholangiogram (IOC). [2,4] The case of Mr U illustrates BDI during laparoscopic cholecystectomy, where disrupted anatomy made identification of structures difficult. This necessitated conversion to an open procedure for confirmation and ultimately a 90% transection of the CBD requiring definitive repair. This article will further examine the role and technique of IOC, outline current management after BDI and will reflect on these in light of recent technical advances.

Case Report

Mr U, a 69 year old man, presented for elective laparoscopic cholecystectomy five weeks after an initial admission for acute cholecystitis. At the time of first presentation, he was managed conservatively due to concurrent acute renal failure and pneumonia, with resolution of his symptoms three days after onset. Later, at surgery, a four-port approach was used to gain access to the abdominal cavity with the anterior liver edge retracted superiorly for exposure of the gallbladder. The gallbladder was fibrotic and shrunken, with significant adhesions formed with both the omentum and the transverse colon. These adhesions disrupted the normal anatomy, distorting the classic appearance of Calot's triangle during the identification of its contributing structures.

At the neck of the gallbladder, a duct structure was identified which appeared to be entering the gallbladder and scissors were used to open the duct longitudinally. Through this defect the lumen was accessed and a cannula inserted distally using a cholangiocatheter grasper. After flow was confirmed with saline, radio-opaque contrast was injected to perform an IOC. The IOC displayed only the lower biliary tree from approximately the midpoint of the CBD to its communication with the duodenum at the Ampulla of Vater. The cannula was removed and re-inserted, and the retracted gallbladder further manipulated to exclude a positional obstruction of the upper biliary tree. When neither of these measures altered the IOC image, the surgery was converted to an open procedure to better define the anatomy. Despite the greater access granted by the open approach, the disruption to the normal anatomy remained significant. Further, a prominent Duct of Luschka obstructed a fundus-first dissection. As a visual determination as to the nature of the cannulated duct was still not possible, the cannula was again re-adjusted for another IOC, without success.



Intraoperative cholangiogram during a laproscopic cholecystectomy.

Although BDI is not a common occurrence, the likelihood that this complication had occurred was now quite high. As such, the cannula was removed from the distal stump and instead inserted into the proximal stump to perform a 'retrograde IOC.' This immediately imaged the upper biliary tree, confirming placement of the cannula within the CBD. Unfortunately, despite only an initially small lateral duct incision, the resulting manipulation and repeated cannulations extended this to approximately a 90% transection. With the CBD imaged via IOC, the anatomy could be better defined and the gallbladder was removed, although the objective at this stage had shifted to minimising bile leak and arranging for repair. An externalised 8 French feeding tube was inserted into the proximal CBD stump and a drain was placed in the subhepatic space prior to closure. Mr U was subsequently transferred to a tertiary hepato-pancreatico-biliary unit for construction of a Roux loop hepaticojejunostomy and was discharged home five days later.

Discussion

Two issues warrant consideration in this case: the role of routine IOC, and minimizing the impact of BDI. Since it was first described, opponents to the routine use of IOC argue that there is insufficient discernable benefit regarding BDI to justify the additional cost and time. [4] This may however be a consequence of small absolute numbers limiting the statistical power of some analyses, particularly given that others have shown that performing an IOC decreases the incidence of major BDI by as much as 40% to 50%. [2,5] Additionally, as many as 69% of cases of iatrogenic BDI are reportedly missed during the initial cholecystectomy, [1] where the use of IOC would allow for early definitive management of these patients. Interestingly, given this debate, a survey of surgeons in Queensland found that 82% currently almost always attempt an IOC in elective cholecystectomy, while less than 4% rarely attempt it. [6]

The majority of cases of BDI in laparoscopy occur when the CBD is mistakenly identified as the cystic duct. [7] In these situations,

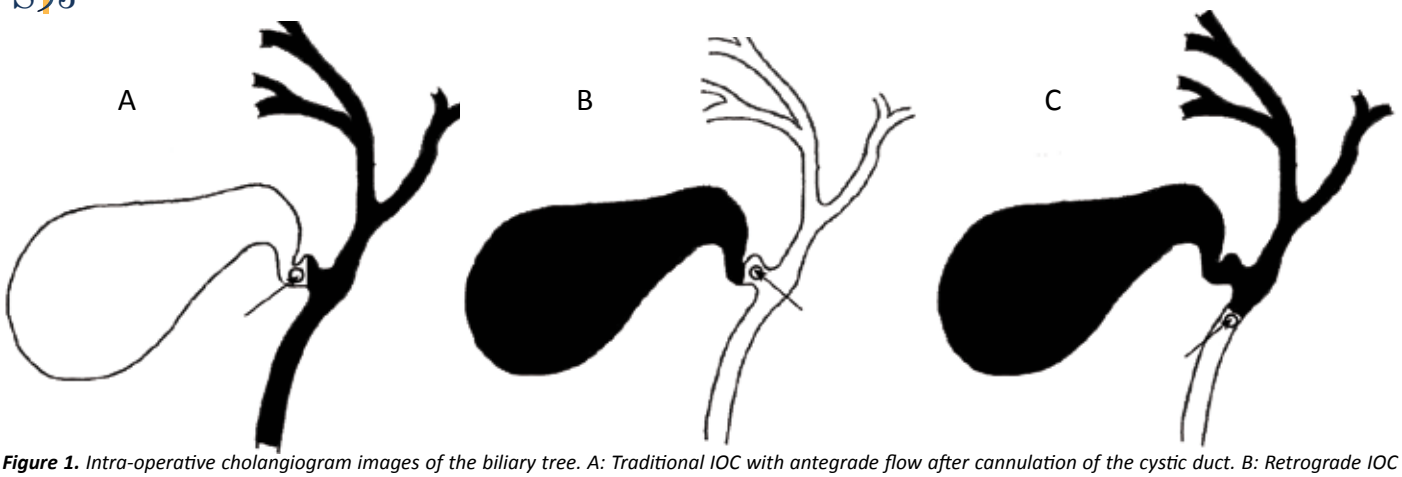


Figure 1. *Intra-operative cholangiogram images of the biliary tree. A: Traditional IOC with antegrade flow after cannulation of the cystic duct. B: Retrograde IOC with retrocgrade flow after cannulation of the cystic duct. C: Retrograde IOC with retrograde flow after cannulation of the common bile duct.*

the injury takes one of two forms: either a Strasberg D or Strasberg E type injury (Table 1). While the use of IOC does not prevent the damage from occurring per se, it does have a marked impact on the ultimate outcome. In limiting the degree of damage to the CBD, IOC allows for success with a less radical repair and ensures that suitable early management is implemented to guard against bile leak and the associated peritonitis or sepsis. [7,8]

The traditional application of IOC is to cannulate the distal opening of the duct accessed by lateral ductotomy. From the cystic duct, radio-opaque dye fills the biliary tree (Figure 1A) providing information on both anatomy and filling defects due to strictures or choledocholithiasis. [2] The dilemma occurs when only the lower ducts are imaged. While this may indicate CBD cannulation, it may also be due to the insertion of the cannula into the cystic duct advanced so far as to enter the CBD, or simply occlusion of the proximal CBD due to stricture or surgical retraction. As in this case, such reasoning may lead the surgeon to manipulate the cannula and surgical field in an attempt to obtain unobstructed flow of the dye into the upper tree, with the potential to worsen the injury. An alternative is the technique adopted later in this case where, when presented with an inability to image the upper biliary tree, the cannula is instead inserted into the proximal opening and a retrograde IOC performed. Placement of the catheter in the cystic duct or CBD produces two different images (Figures 1B and 1C), allowing a determination as to whether a BDI has occurred.

Table 1. *Strasberg classification of bile duct injuries. [3]*

Class of injury	Discription	Possible circumstance of injury
A	Leak from small ducts still in continuity with the biliary tree	Presence of small accessory ducts from liver bed or cystic duct
B	Injury to a sectoral duct with obstruction to drainage of that part of the biliary tree	Presence of an aberrant right hepatic duct
C	Injury to the sectoral duct with bile leakage from that duct which is not in continuity with the tree	Presence of an aberrant right hepatic duct
D	Partial lateral injury to the common bile duct	Lateral injury in preparation for insertion of catheter for IOC [2, 10]
E	Ranges from stricture to complete obstruction to the common bile duct	Complete transaction in preparation for dissection of gallbladder [10]

This potentially has the advantage of minimising any further damage to the bile duct which could occur during manipulation or repeated re-cannulation of the distal stump.

Ultimately, this may influence the options and success of the repair process as the degree of injury determines the management options available. If the CBD has undergone only a lateral injury during cannulation (Strasberg D), then management either by suture over a T tube or during endoscopic retrograde cholangio-pancreatography (ERCP) is likely to be successful. [7] This is in comparison to a complete transection (Strasberg E), for which the current accepted treatment in most cases is the creation of a Roux-en-Y hepaticojejunostomy. [8] Although studies have demonstrated success rates of more than 90% for a Roux-en-Y, [9,10] failures have occurred after more than seven years [9] and thus ongoing follow-up is essential.

Furthermore, it has been demonstrated that in specialised centres, a laparoscopic hepaticojejunostomy can be employed successfully for repair of major BDI [11] with repairs of more minor injuries already suited to minimally invasive repair, particularly endoscopic stenting. [1] Therefore, at the time of injury, a retrograde IOC could be performed laparoscopically in preference to conversion to an open exploration. Although not adopted in this case, this may provide the patient an opportunity to avoid an open operation entirely and with that, benefit from the advantages commonly associated with minimally invasive techniques, including decreased post-operative pain and better cosmetic results. [12]

While the retrograde application of IOC does offer many advantages, its feasibility for application in clinical practice may face a number of readily identifiable hurdles. For example, in order to image upstream from the site of the ductotomy, proximal clips need to be removed, risking bile leakage and escape of gallstones into the peritoneal cavity. Additionally, if the cannula is correctly placed but the cystic duct is obstructed by an impacted gallstone – not an altogether unexpected finding in patients undergoing cholecystectomy – the inability to achieve free flow may prompt repeated cannulation attempts, resulting in the very damage this technique seeks to avoid. Fortunately, a completely obstructed proximal duct is very unlikely to occur without significant derangement to pre-operative liver function tests. Finally, while cannulation of the proximal stump was readily achieved after conversion to open access in this case, suitable anatomy, particularly during laparoscopy, may not always be present. In summary, while this approach may not be suitable in all cases, its utilisation should be attempted given the potential advantages to both surgeon and patient.

Conclusion

In laparoscopic cholecystectomy, particularly where the normal anatomy is disrupted, IOC has been shown to decrease major iatrogenic injury to the bile duct. When a standard IOC fails to image the upper biliary tree, the laparoscopic cannulation of the proximal stump for a retrograde IOC should be attempted. Where successful,

this would allow for rapid detection of a BDI and the institution of early damage minimisation measures and definitive repair. This may ultimately provide a better prognosis through preventing extension beyond a lateral injury and avoidance of an open procedure entirely, as laparoscopic hepaticojejunostomy is now technically feasible.

Conflict of interest

None declared.

Consent

Informed consent was obtained from the patient for publication of this case.

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Minimally invasive mitral valve repair: A new surgical option for mitral insufficiency

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Minimally invasive mitral valve repair (MIMVR) is a relatively new alternative to median sternotomy for valvular heart surgery, and has become increasingly appealing due to its improved cosmetic results and more rapid recovery time. Patients suffering mitral valve disease are increasingly turning to their medical practitioners for advice regarding this procedure. It is the aim of this article to provide a review of MIMVR to allow students and doctors to better understand this recent development in cardiac surgical therapy.

Introduction

Mitral valve incompetence is characterised by 'ballooning' or prolapse of the mitral valve, followed by the eventual retrograde flow of blood into the left atrium during ventricular systole. Most commonly caused by degenerative, rheumatic, ischaemic or infectious pathological processes, 2,182 Australians were diagnosed with mitral valve insufficiency and 370 with mitral valve prolapse in 2004/05. [1,2] Congenital deformities, endocardial lesions, cardiomyopathies and connective tissue disorders are less frequent triggers of disordered mitral valve function. [1]

Degenerative changes are the most common cause of mitral insufficiency, resulting in a range of conditions including mitral valve prolapse, insufficiency ('floppy valve syndrome') and, in a minority of patients, severe mitral regurgitation (due to rupture of the chordae tendineae, dilatation of the mitral valve annulus or a combination of both complications) (Figure 1).

Chronic rheumatic heart disease is a common cause of mitral valve disorders in Aboriginal and Torres Strait Islander populations, with a prevalence of 16.6 per 1,000 population in the Top End of the Northern Territory and 12.5 per 1,000 in Central Australia, compared with respective figures of 1.7 per 1,000 and 0.6 per 1,000 amongst other Australians. [3] Although more commonly associated with mitral stenosis, rheumatic heart disease may result in a combined stenosis and insufficiency, or occasionally, an isolated rheumatic insufficiency. [1]

Whatever the cause, mitral valve insufficiency ultimately results in retrograde flow of blood from the left ventricle (LV) to the left atrium during left ventricular systole, leading to a volume overload of the left atrial chamber. The response of the myocardium varies depending on the pathophysiological syndrome present when regurgitation occurs. In acute severe mitral regurgitation, the sudden volume overload of the left atrium and left ventricle precludes the development of compensatory eccentric hypertrophy (due to the rapid nature of the condition), with a consequent simultaneous reduction of forward cardiac output and pulmonary congestion.

The patient presents with severe symptoms including dyspnoea, a systolic murmur (although it may not be pansystolic and occasionally may be absent) and an S3 heart sound or early diastolic rumble. [4] In comparison, the myocardium of patients experiencing a chronic, mild mitral regurgitation will undergo eccentric hypertrophy, resulting in a compensatory increase in end-diastolic volume that results in an increased stroke volume and restoration of cardiac output. [4]

Eventually, these patients will experience left ventricular decompensation, with a considerably reduced systolic ejection capability. This results in a reduced forward output, often with an ejection fraction in the lower normal range (EF 0.50-0.60), [4] and consequent volume overload of the left atrium with left atrial dilatation and potentially the development of atrial fibrillation. LV dysfunction and left atrial volume overload also generate a retrograde pressure gradient through the pulmonary circulation, resulting in pulmonary congestion, and respiratory signs of heart failure. Physical examination of patients with chronic asymptomatic mitral regurgitation frequently demonstrates displacement of the apex beat due to eccentric hypertrophy and possibly a palpable heave. An S3 heart sound is usually present and there may be a pansystolic murmur. Findings indicative of the development of pulmonary hypertension in these patients are suggestive of an advanced disease state and worsening prognosis. [4]

Diagnosis of mitral valve insufficiency is based on symptoms, physical findings and two-dimensional and Doppler echocardiography indicating a leaflet thickness of >5mm and/or leaflet prolapsed >2mm. [4]

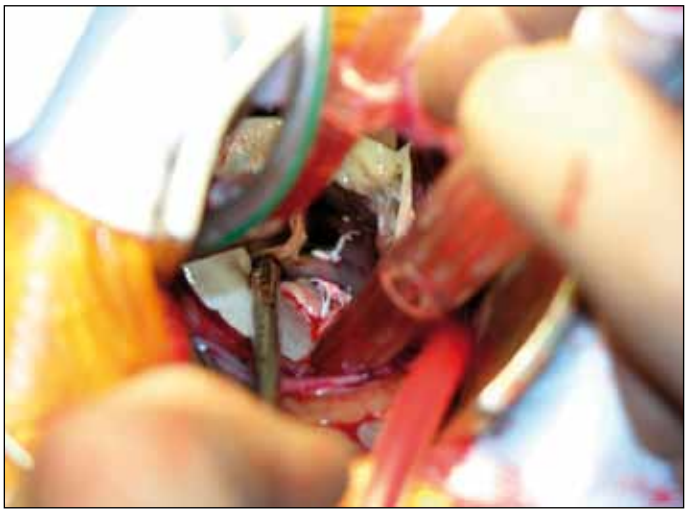

Figure 1. *Long-shafted instruments in use during mitral valve repair.*

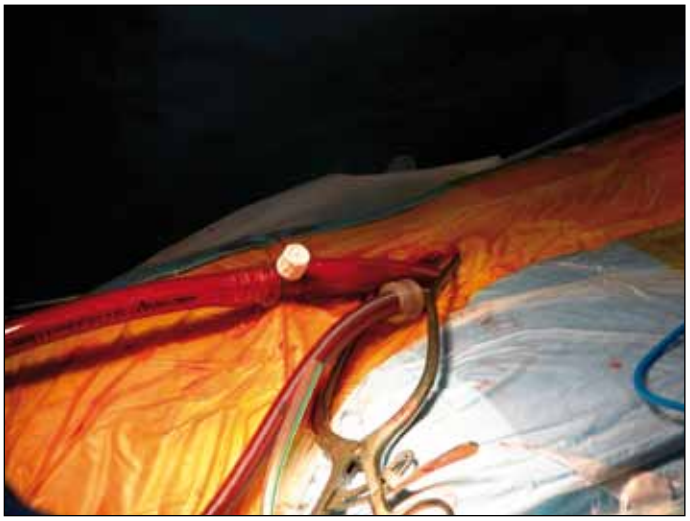

Figure 2. *Femoro-femoral bypass cannulae in situ.*

Minimally invasive mitral valve surgery

Currently, there are three different operations performed for mitral regurgitation: repair, replacement with preservation of the mitral structures, or replacement with removal of the mitral structures.

The indications of mitral valve surgery are:

- Symptomatic acute severe mitral regurgitation.
- Chronic severe mitral regurgitation with at least one of the following:
  - NYHA functional class II, III, IV symptoms in the absence of severe LV dysfunction (severe LV dysfunction defined as EF <0.30) and/or end-systolic dimension >55mm; or
  - Asymptomatic with mild to moderate LV dysfunction, EF 0.30 – 0.60 and/or end-systolic dimension >/= 40mm; or
  - Asymptomatic chronic severe mitral regurgitation with preserved LV function and new; or
  - Asymptomatic chronic severe mitral regurgitation with preserved LV function and pulmonary hypertension (Pulmonary artery systolic pressure >50mmHg at rest or >60mmHg with exercise).
  - Chronic severe mitral regurgitation due to a primary abnormality of mitral apparatus and NYHA classification III-IV symptoms with severe LV dysfunction (EF <0.30 and/or end-systolic dimension >55mm) in whom mitral valve repair is highly likely.

Mitral valve repair may be considered in:

- Severe chronic mitral regurgitation, requiring surgery.
- Asymptomatic chronic severe mitral regurgitation with preserved LV function (EF >o.60 & end-systolic dimension <40mm).
- Chronic severe secondary mitral regurgitation due to severe LV dysfunction, with persistent NYHA class III-IV symptoms despite optimal heart failure therapy, including bi-ventricular pacing.

The midline sternotomy remains the most common incision in cardiothoracic surgery, offering excellent access to all intrathoracic structures. It currently remains the standard approach for aortic and mitral valve surgery. [5]

Minimally invasive mitral valve surgery, specifically port-access mitral valve surgery, is a video-assisted endoscopic technique allowing mitral valve replacement or repair (valvuloplasty and/or annuloplasty) via a series of intercostal ports, thus removing the need for median sternotomy. [5-9]

The minimally invasive technique described is based on the use of the EndoCPB© endovascular cardiopulmonary bypass system, created by Heartport Inc (Redwood City, CA, USA). It is based on initial experience

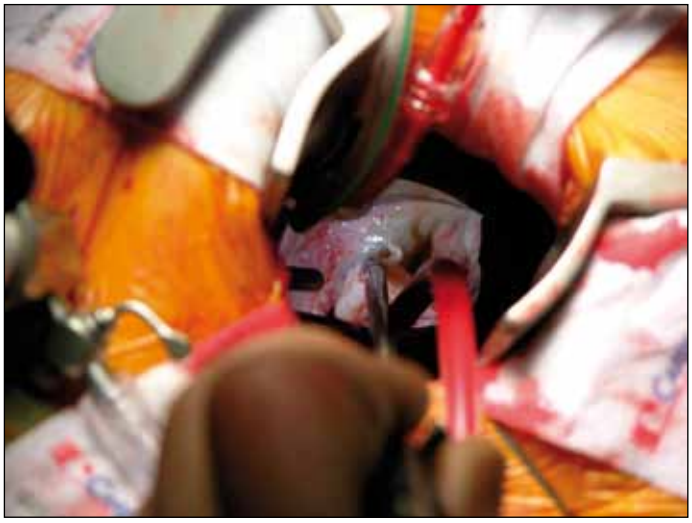

Figure 3. *Surgeon's view through left-sided atriotomy showing the mitral valve in the centre of the picture.*

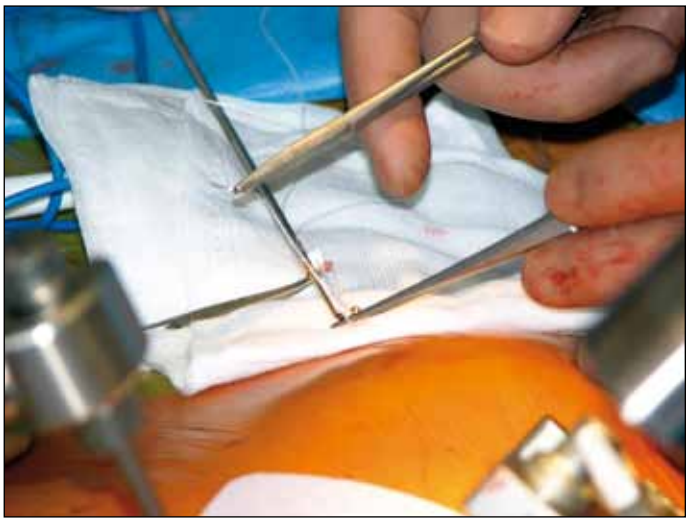

Figure 3. *Preparation of Gore-Tex sutures measured against long-arm callipers.*

with the Da Vinci Robotic Surgical System, which may be used to perform minimally invasive mitral valve repair. The technique outlined below does not use the Da Vinci system, instead being performed directly by the surgeon utilising specific long-shafted instruments (Figure 2).

Pre-operative assessment of vascular status is important as use of the EndoCPB© system may be contraindicated in some patients with peripheral vascular disease. [6] Physical examination and Doppler sonography remain the mainstay of pre-operative vascular assessment.

Intubation is performed by a qualified cardiothoracic anaesthetist with a double-lumen endotracheal tube. The patient is placed in the dorsal decubitus position and transoesophageal echocardiography is commenced. Femoral cutdown is performed and access is gained to the jugular vein, allowing placement of cannulae for femoro-femoral cardiopulmonary bypass (Figure 3) and endocoronary sinus catheter placement respectively. [5,7,8]

Once cardiopulmonary bypass cannulae are in place, a 4-5cm incision is made in the skin of the right inframammary groove, and a port is created in the fourth intercostal space. Soft tissue retractors are then used to retract the soft tissues, providing access to the thoracic cavity (Figure 4). [5-9] A second port is created in the third intercostal space to allow access for the thoracoscope.

The ascending aorta is clamped and retrograde cardioplegia delivered to the heart. Aortic clamping is obtained through the use of either a standard aortic cross-clamp at the root of the aorta or an endoaortic balloon clamp that also allows monitoring of aortic root pressure.

Table 1. *The benefits of minimally invasive mitral valve repair, as compared to conventional surgical approaches.*

Benefits of MIMVR
Smaller incision (4-5cm)
Avoids sternotomy
More rapid return to normal activity
Reduced pain
Reduced incidence of sepsis and wound infection
Reduced occurrence of new-onset atrial fibrillation
Shorter hospital stay
Lower requirement for transfusion
Lower mortality
Improved patient satisfaction
Reduced costs

Surgical access to the mitral valve is gained via a left atriotomy, allowing the surgeon to look down through the lumen of the valve into the left ventricle (Figure 5). The damage to the valve can then be assessed visually, and repaired through valvuloplasty, chordal repair or annuloplasty. Ruptured chordae tendineae can be excised and replaced by Dacron suturing measured against the distance from valve leaflet to papillary muscle by long-arm suture calipers. If annuloplasty is required, the valve size is measured using a valve sizer, and an annuloplasty ring lowered to the atrial surface of the valve. The atriotomy is then closed, the patient placed in the Trendelenburg and lateral decubitus positions, and de-airing commenced. Heartbeat is resumed, and the patient is weaned from cardiopulmonary bypass prior to transfer to the intensive care unit. [5-9]

Discussion

Minimally invasive mitral valve repair (MIMVR) is an evolving procedure that, although developed in 1996, [5] is now coming to play a large part in the surgical management of valvular heart disease.

While no thorough analyses have been completed by government or clinical authorities (such as the UK National Institute of Clinical Excellence or the Australian Safety and Efficacy Register of New Interventional Procedures - Surgical), original research suggests that MIMVR is a viable and safe alternative to standard median sternotomy for mitral valve surgery, conferring a multitude of benefits to the patient (Table 1). [5-16]

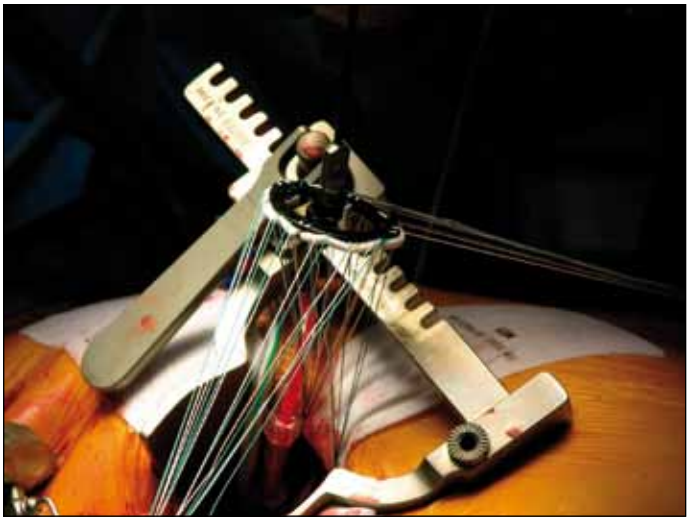

Figure 5. *Insertion of annuloplasty ring.*

Yet despite its multiple benefits, reduced costs and improved cosmetics, MIMVR has its own unique set of potential complications. By 1999 there had been 25 reported cases of retrograde aortic dissection worldwide associated with surgery. Potential exists for cerebrovascular accident (occurring in 0.6% of cases in the port-access international registry). The endoaortic balloon may migrate to the aortic valve, perforate, or be captured during suturing. Femoral arterial cannulation may prove to be impossible in some patients necessitating a change of procedure to median sternotomy. Other potential complications include kinking or obstruction of the venous cannulae inadvertent placement of the venous cannula in the superior vena cava and perforation of the coronary sinus, right atrium by a guidewire or of the left atrium via an atrial septal defect. [5,14]

Overall however, MIMVR is held to be a viable alternative to median sternotomy, with a comparable level of clinical safety. [5-16] Data from one study suggests that MIMVR is associated with a lower morbidity and shorter hospital stay in elderly patients when compared to standard mitral valve replacement via median sternotomy. [13] Whilst one prospective, randomised study suggested that there were no significant advantages of minimally invasive port access technique over median sternotomy, and that MIMVR was associated with a longer operating time and more intraoperative procedure-related problems, the authors conceded that their study was limited by their own experience with minimally invasive techniques. Further, the small sample sizes of their groups restricted their ability to detect statistically significant differences in clinical, biochemical and neuropsychological variables. [15]

Conclusion

MIMVR is a safe, viable alternative to median sternotomy in patients with adequate peripheral vasculature, and offers significant advantages in terms of morbidity, cost, patient satisfaction and cosmetics when performed by experienced practitioners.

Conflict of Interest

None declared.

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Ovarian carcinoma: Classification and screening challenges

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Primary ovarian cancer is the leading cause of death from gynaecological malignancy and the sixth most common cause of cancer death in Australian women. Our understanding of the underlying pathophysiology of epithelial ovarian cancers is incomplete, which poses difficulties for screening, diagnosis and treatment. This review summarises the current knowledge and debate regarding classification of epithelial ovarian cancers, including a proposed new classification system. Current screening methods and the evidence behind them are also presented. The outcomes of large, ongoing trials are awaited to provide more conclusive evidence regarding the effectiveness of screening for ovarian cancer.

Introduction

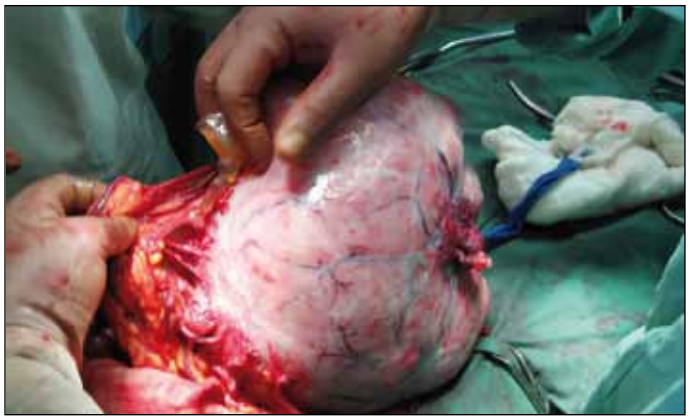
Primary ovarian cancer is the leading cause of death from gynaecological malignancy, and the sixth most common cause of death from cancer in Australian women. Mortality is high, with five year survival rates of only 42%. Ovarian cancer is staged according to the extent of disease spread. Stage I disease is confined to the ovaries, while stage II involves extension into the pelvis. Stage III is characterised by disease with peritoneal implants outside the pelvis or nodal involvement of retroperitoneal or inguinal lymph nodes. Stage IV describes disease with distant metastases. Symptoms are non-specific and often occur late in disease such that 53% of women diagnosed with ovarian cancer present with stage IV disease. Since five year survival drops from 86.1% for stage I disease to only 7% for stage IV disease, early diagnosis is important. [1,2] Unfortunately, the current lack of knowledge regarding the pathophysiology of ovarian cancer poses challenges for the classification of these cancers and therefore the implementation of optimal screening programs.

Classification of epithelial ovarian cancers

Primary ovarian malignancies are broadly classified as either epithelial, germ cell or sex cord stromal, with over 90% being of the epithelial type. [2] Germ cell and sex cord stromal tumours show different pathogenesis, epidemiology, clinical management and outcomes and are not addressed in this review.

The classification of epithelial ovarian carcinomas remains somewhat controversial in that the current system may not adequately describe the underlying cellular origins, pathological process or disease prognosis. [3] These tumours are generally classified as one of four major types according to their morphology – serous, mucinous, endometrioid and clear cell, with each of these histological types representing an organ of the female reproductive tract. Serous and mucinous types resemble fallopian tube and endocervix respectively, while endometrioid and clear cell tumours resemble the endometrium. Tumours can be further typed according to whether they are benign cystadenomas, malignant carcinomas or tumours of low malignant potential, also termed borderline tumours or atypical proliferative tumours. [4]

The cellular origin of epithelial ovarian carcinoma is not entirely understood and this poses difficulties for accurate classification. The wide-held belief is that these tumours arise from ovarian surface epithelium or, more specifically, from inclusion cysts formed from invaginations of the epithelium which lose their continuity with the surface. [4] Ovarian epithelium is derived from the embryonic coelomic mesothelium, as is the peritoneum, pericardium and pleura. However, it is controversial as to whether this adequately explains the histological similarity of ovarian tumours to organs derived from the Müllerian ducts. The Müllerian ducts are classically thought to arise from invagination of the coelomic epithelium, which might explain their histological similarities. However, histological analyses of human embryos have suggested that this may not be the case entirely. It appears that the development of the Müllerian duct may be closely related to that of the Wolffian duct, with Müllerian duct growth being independent of the invagination of coelomic epithelium. Cells of the Müllerian epithelium can be readily distinguished from coelomic cells and Wolffian cells. [5] Debeau [6] hypothesises that epithelial ovarian carcinomas may in fact be of Müllerian origin. Similarly, Kindelberger *et al.* [7] suggest that ovarian carcinomas, particularly those of the serous subtype, may arise from the fimbriae of the fallopian tube.



Removal of a large ovarian tumour.

In addition to the existing controversy regarding cellular origins, the advent of molecular genetic testing technologies has led to increased debate regarding the accuracy of the traditional classification system. Shih and Kurman [3] propose an updated classification to take into account the clinicopathological behaviour, tumour progression and molecular genetics of epithelial ovarian carcinomas, with the aim of providing a better framework for research into screening and treatment strategies.

They propose a novel tumour progression model whereby tumours are broadly grouped as type I or type II tumours. Type I tumours are generally low-grade and arise from precursor lesions with known molecular genetic alterations. These include low-grade serous carcinoma, mucinous carcinoma, endometrioid carcinoma and clear cell carcinoma. Type II tumours include high-grade serous carcinoma, undifferentiated carcinoma and malignant mixed mesodermal tumour (carcinosarcomas), and are characterized by having no known precursor lesion and poorly defined genetic alterations, aside from a common *p53* mutation. Such tumours often present as advanced stage IV tumours at the time of diagnosis and presumably undergo rapid growth from an occult lesion to a clinically detectable carcinoma. Table I outlines the classification and characteristics of type I and type II tumours. There is a notable difference in the known genetic mutations between type I and type II tumours, suggesting separate underlying pathogenic processes. This may provide a possible avenue for future screening, diagnosis and treatment investigations. [3] This classification system has not gained widespread acceptance for the

Table 1. A novel classification system - type I and type II epithelial ovarian carcinomas, their precursor lesions and common genetic mutations. [3]

	Tumour Type	Precursor Lesion	Molecular Genetic Mutations
Type I	Low-grade serous carcinoma	Serous cystadenoma/ adenofibroma; borderline serous tumour	BRAF and KRAS (~67%)
	Mucinous carcinoma	Mucinous cystadenoma; borderline mucinous tumour	KRAS >60%
	Endometrioid carcinoma	Endometriosis; endometrioid adenofibroma; borderline endometrial tumour	Loss of heterozygosity or mutation in PTEN (20%); β-catenin gene (16-45%); KRAS (4-5%); microsatellite instability (13-50%)
	Clear Cell Carcinoma	Endometriosis; clear cell adenofibroma; borderline clear cell tumour	KRAS (5-16%); microsatellite instability (~13%); TGF-β RII mutation (66%)
Type II	High-grade serous carcinoma	Not yet identified	P53 mutations (50-80%); amplification and overexpression of HER2/neu gene (10-20%) and AKT2 gene (12-18%)
	Undifferentiated carcinoma	Not yet identified	Not yet identified
	Malignant mixed mesodermal tumour (carcinosarcoma)	Not yet identified	P53 mutations (>90%)

classification of ovarian malignancies.

Evidence-based review of screening processes and limitations of screening

According to the World Health Organisation (WHO), screening programs should be supported by sufficient scientific evidence and the screening initiative should incorporate education, testing, clinical services and program management. There should be quality assurance, informed consent, equitable access, confidentiality and respect for autonomy. Additionally, the benefits of screening should not outweigh the harm. [8]

Ovarian cancer is a disease with high mortality which may be decreased by early intervention since five year survival is in excess of 80 % when the disease is confined to the ovaries. [2] Although ovarian cancer screening is a recognised need, there are a number of challenges in fulfilling the abovementioned WHO criteria. Limited knowledge of the natural history of the disease has thus far prevented the identification of suitable populations for screening.

Until further research can confirm the tumour progression model proposed by Shih and Kurman, [3] a true precursor lesion is yet to be clearly identified. A number of biomarkers have shown promise in samples from known ovarian cancer patients but few have been thoroughly studied in the preclinical phase as screening tools. Blood tests for the tumour marker CA125 and pelvic ultrasound have been the most studied screening techniques. In combination, they can detect a significant proportion of preclinical cancers and may improve survival. However, our understanding of the biology of ovarian cancer cannot yet fully describe how or whether stage I disease progresses to stage IV disease. [9] Thus, it remains unclear as to whether early detection and intervention would to be able to alter the natural history of the disease, nor has there been evidence as yet to demonstrate that screening decreases mortality. Other challenges relate to sensitivity, specificity, cost, exact screening protocol, acceptability and compliance. [10,11]

CA125 blood tests and pelvic ultrasound have been the most widely studied screening tools for ovarian cancer, with large-scale trials still underway. CA125 is an antigen expressed by foetal coelomic and amniotic epithelium. In adults, it is found in tissues derived from coelomic epithelium (pleura, pericardium and peritoneum) and Müllerian epithelium (tubal, endometrial, cervical). While ovarian epithelium does not normally express CA125, expression is often a feature seen in inclusion cysts and metaplasia. The cut-off for a positive screen is > 35 U/L, which is present in over 50% of patients with stage I disease and over 90% of patients with more advanced disease. [10] Studies have also shown that CA125 may be detectable in the preclinical phase, with elevated levels found in 25% of stored samples collected five years prior to diagnosis of ovarian cancer. [12]

Unfortunately, the false positive rates associated with CA125 testing on its own are quite high since elevations are also seen in cancers of the prostate, breast, bladder, liver and lung, and benign diseases such as diverticulitis, fibroids, endometriosis, ovarian cysts and tubo-ovarian abscess. [10]

Pelvic ultrasound is aimed at detecting early morphological changes. Unfortunately, there is no standardised scoring index for ultrasound findings but many are based on ovarian volume, outline, presence of papillary projections and cyst complexity (number of locules, thickness of septae, wall structure and echogenicity of fluid). In terms of these criteria, papillary projections have the highest and simple cysts and septal thickness have the lowest correlation with malignancy. There was hope that Doppler scanning could provide better sensitivity and specificity by differentiating between benign and malignant lesions on the basis of blood flow and vascular resistance, but due to the degree of similarity between the two, this was not proven to be effective. [10] While transvaginal ultrasound offers better visualisation of the ovaries compared to transabdominal ultrasound, it still cannot be used to clearly distinguish between benign and malignant lesions. [2]

Due to the likely short time interval between malignant change and widespread disease, particularly in high-grade tumours, screening efficacy is questionable. A recent study by Brown and Palmer [13] analysed serous cancers found after prophylactic bilateral salpingo-oopherectomies in BRCA1 carriers. They found that these cancers spend approximately four years as in situ stage I or stage II cancers and a further one year as stage II and III before becoming clinically apparent. For most of this occult period, the cancers are less than 1 cm in diameter and not grossly visible. Thus, to detect serous carcinomas before stage II, disease testing would need to detect tumours of 1.3 cm with a specificity of 50%, and tumours of less than 0.4 cm with a specificity of 80%. To achieve a 50% reduction in mortality with an annual screen, they postulate that screening would need to detect tumours as small as 0.5 cm in diameter. As such, although there is a relatively long occult period, current screening with CA125 and pelvic ultrasound is not adequately sensitive nor specific. It is likely that population screening will require additional cancer-specific biomarkers or novel approaches.

Ideally, the specificity of screening tests for ovarian cancer should be high to minimise morbidity from invasive testing in false-positive women. There are currently no reports on quality of life in such women. It is generally agreed that a screening test must have at least 10% positive predictive value (PPV), that is, no more than nine false positives for every one true positive. Given a population incidence of 40 cases per 100,000 population per year for ovarian cancer, tests would require a sensitivity of 75% and specificity of 99.6% to achieve a PPV of 10%. As this is a challenge for any single biomarker, it is likely

that any screening protocol will require a combination of tests. [10]

Another challenge in ovarian cancer screening is determining appropriate target population groups for screening. Most ovarian cancers occur sporadically with the only risk factor being age over 50 years. Women at increased risk of developing ovarian cancer only account for 5-10% of ovarian cancers, and include women with a family history of ovarian cancer, BRCA1/2 carriers and HNPCC carriers. Their risk can be considerably high, with a cumulative risk of 39% by age 70 in BRCA1 carriers. [10] Screening in these women is generally recommended from age 35, although this practice is not supported by evidence. Genetic counselling is also required where a known gene mutation exists. [14] The difficulty with screening these women is that they are usually younger and often have a variety of physiological (menstrual cycle variations) and benign (endometriosis, ovarian cysts) conditions which affect CA125 levels and ultrasound findings. Studies are required to assess whether serial CA125 measurements may be useful in such groups. [10]

Most biomarkers are initially tested in women with clinically diagnosed and usually advanced stage cancers. While they may show high sensitivity in these populations, the challenge is to find a biomarker which is also elevated in preclinical disease. [10] As CA125 is currently the best studied biomarker, it is likely to form a part of screening protocols in the near future. A number of studies have aimed to assess its effectiveness as a screening tool. Jacobs *et al.* [15] assessed the performance of CA125 followed by ultrasound in screening for ovarian cancer. They recruited 22,000 postmenopausal, female volunteers aged over 45 and measured their CA125 level. Abdominal ultrasound was performed if the level was ≥30 U/ml and abnormal ultrasound results were referred for surgical investigation. Of the 22,000 women, 40 required surgical investigation – eleven of these had disease while the remaining 30 had benign or no lesions present. Of the 21,959 women who had a negative screening result, eight subsequently presented clinically with ovarian cancer (false negative) and 21,951 had not developed clinical cancer in the two year follow up period. Sensitivity was thus 99.9%, PPV 26.8% and apparent sensitivity was 78.6% at 1 year and 57.9% at two years. As this was a prevalence study, information regarding the value of this screening protocol as ongoing screening was not available. However it does suggest that a screening interval of just 1 year may be required, which has potential implications on the cost, acceptability and compliance of screening. [11,15,16] In 2003, Skates *et al.* [17] used data from the Jacobs trial [15] to show that serial CA125 measurement interpreted with risk calculation was more effective in screening for ovarian cancer than a single, fixed cut-off measurement for CA125. The risk calculation is an estimate of the probability of having preclinical ovarian cancer and takes into account age and pattern of CA125 values. For a target specificity of 98%, the risk calculation achieved a sensitivity of 86%, whereas use of a fixed cut-off was only 62% sensitive. [17]

The UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) is a large, ongoing trial to assess the effectiveness of ovarian cancer screening on mortality. While the final results are still several years away, the results from the initial screen are promising. Over 200,000 post-menopausal women were randomly allocated to either receive no screening, annual CA125 with second-line transvaginal ultrasound, or annual transvaginal ultrasound alone. The sensitivity, specificity and positive predictive value for all primary ovarian and tubal cancers were 89.4%, 99.8% and 43.3% for multimodal screening and 84.9%, 98.2% and 5.3% for ultrasound screening respectively. There was a significant difference in specificity but not sensitivity between the two modalities. [18] Since PPV should be greater than 10% for an effective screening test to minimise morbidity from investigating false negatives, multimodal screening appears to be superior. Of the 87 malignancies found across both groups, there was no stage distribution difference found between the groups – overall, 48.3% were stage I or II. All of the cancers found in the ultrasound group were found from abnormalities on the first screen whereas only 78.6% of cancers from the multimodal screening arm were found on the initial test and 21.4% from an initial indeterminate screening result that required further testing, resulting in a delayed diagnosis for these women. Despite this, multimodal screening did result in fewer repeat tests and almost nine times fewer operations per cancer found. Results are awaited of further screening to assess ongoing sensitivity, specificity and PPV. [18]

Conclusion

In summary, ovarian cancer remains an important health issue with a number of challenges remaining for screening and diagnosis. Consensus is needed regarding a classification system – this is likely to require further study into the pathological basis of disease in serous ovarian cancer. Following this, efforts to find screening modalities which are sensitive, specific, cost-effective, acceptable and which lower mortality are required. This may be possible by refining CA125 and ultrasound modalities or it may require a novel approach. The main issues with screening stem from the lack of a clearly defined precursor lesion, and a lack of evidence to suggest that screening reduces mortality. Consequently, screening of the general population for ovarian cancer in Australia is currently not recommended.

Conflicts Of Interest

None declared.

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Novel approaches to cancer therapeutics

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Advancements in our understanding of the biology of cancer have progressed dramatically over the past decade. The application of cutting-edge molecular profiling techniques analysing the cancer genome is elucidating an appreciable amount of information. This data is now being integrated into a catalogue that is providing researchers with a revolutionary roadmap of the molecular mechanisms behind cancer. Recent accomplishments in cancer research are also being introduced into the clinic through the development of innovative diagnostic technologies and targeted therapies. Lessons from the past, along with novel therapeutic approaches being developed today, have stimulated an optimistic promise for tomorrow's fight against cancer.

Introduction

Cancer has the largest burden of disease on the health care system in Australia. [1] Over 100,000 new cases were diagnosed nation-wide in 2005 and the incidence projections from 2006 through 2010 are expected to grow by over 3000 cases annually. [1] Combinations of surgery, radiation and chemotherapy are the most applied treatment modalities in cancer. Unfortunately, surgery and radiation are often palliative interventions for metastasising cancers and the number of systemic treatment options available for cancer is relatively limited. Many current chemotherapeutic treatments for cancer use the 'shotgun' approach, which targets DNA replication with an attempt to exploit the high rates of cell division, a concept that was discovered over 50 years ago and has since changed very little. [2] However, a revolution in the methodology applied to modern molecular medicine is elucidating fundamental characteristics of the genetics behind cancer, providing researchers with a 'molecular handle' to develop novel targeted systemic therapeutic strategies.

The advent of the human genome project sprouted a revolution in '-omics' technologies which accelerated our comprehension of the molecular mechanisms involved in health and disease. Cancer is no exception. The biotechnology industry is now developing novel diagnostic microarray technologies capable of characterising the extensive variability of cancer genetics between patients with considerable accuracy and detail, while the pharmaceutical industry is racing to fill the pipeline with targeted molecular therapeutic agents never before used clinically. [2-4] Together, 'personalised' diagnostic analyses in partnership with a new generation of drugs have the potential to change the way cancer is treated and subsequently improve patient outcomes and survival. Armed with the right tools, tomorrow's clinicians could become well equipped cancer-killing assassins.

Molecular profiling and tools in the making

In 1975, a technique called Southern Blotting was developed which exploited the A-T G-C sequence-specific hybridisation of DNA. This efficiently enabled the specific identification of individual gene sequences. [5] This approach is now being applied in a novel way to gene chips, or microarrays. Microarrays containing thousands of specific gene sequences are capable of identifying specific genomic changes and allow visualisation of entire gene expression profiles of cells under a given set of conditions. [3,6,7] For example, a cell under normal conditions without any stressors or stimulants will express a particular set of "housekeeping" genes for optimising survival through the regulation of mRNA transcription. The relative levels of mRNA

transcripts can be visualised, monitored and catalogued for future reference using microarray-based gene expression profiling. [3,6,7] The expression profiles of cancer cells can then be tested in real time under various conditions for comparison against the reference catalogues. [6] The differences between the two expression profiles can be used to identify changes in gene activation in carcinogenesis.

Tumours are traditionally classified by histology, which enables the crude prediction of characteristics and prognosis of a cancer. Microarray analyses of cancers have demonstrated that tumours with

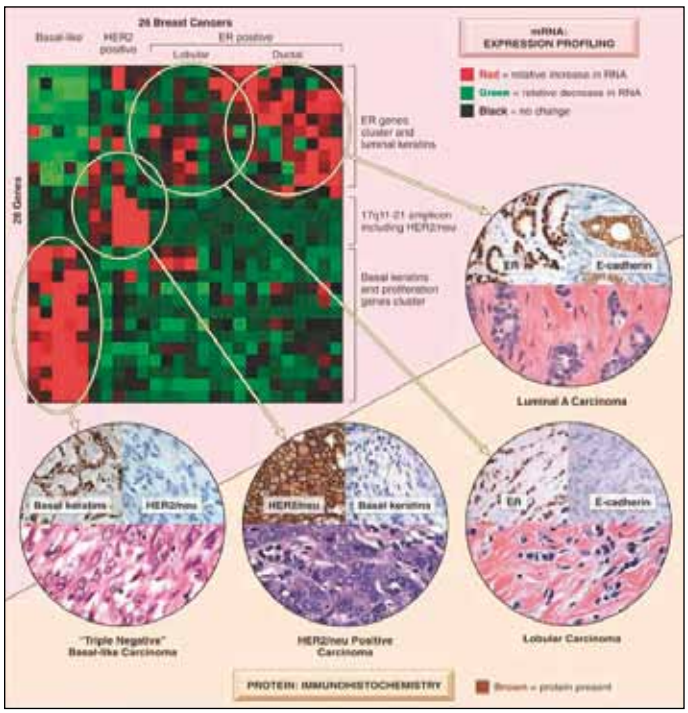

Figure 1. *Gene expression portraits of breast carcinomas. Alterations in mRNA and protein expression identify breast cancer subtypes previously recognized by morphology (e.g., lobular carcinomas) and define new subtypes ("luminal A," "HER2/neu positive," and "basal-like"). [10] (Array data courtesy of Dr. Andrea Richardson, Brigham and Women's Hospital, Boston, MA, as modified from Signoretti S, Di Marcotullio L, Richardson A, Ramaswamy S, Isaac B, Rue M et al. Oncogenic role of the ubiquitin ligase subunit skp2 in human breast cancer. J Clin Invest 2002;110:633. This image was published in Robbins and Cotran Pathological Basis of Disease, 8th Edition, Kumar* et al.*, Copyright, 2009, Saunders, an imprint of Elsevier. Used with permission.)*

histological similarity can develop from distinct genetic mechanisms which influence the progression of disease. [2,3,8,9] Figure 1 demonstrates the conjoining of histological analyses with microarrays, allowing greater accuracy in the characterisation of disparate types of cancer. [2,3,8-10]

Gene expression profiles are also divulging information about the susceptibility of tumours to different targeted chemotherapeutic agents which can help clinicians decide on the most effective treatments. [2,3,8-10] This is the basis of personalised therapeutics.

Following suit with these genomic technologies are proteomics and metabolomics, which utilize analytical methods to monitor the set of proteins and metabolites within a cell. [4,6] Collectively, these techniques have many implications in modern medicine. For example, they allow the analysis of the effects of various drug compounds on different cell types or the precise characterisation of specific tumours or other cells in diseased states. [4,6] The applications of molecular profiling technologies such as these have the potential to increase the rate of success of drug discovery and development. By predicting drug response and toxicity before the compound ever enters clinical trials, failure rates and overall development costs would ultimately be reduced. [3,11]

The first eukaryotic gene expression microarray was developed in 1997 and now, more than a decade later, this technology is eliciting an immense amount of data about the molecular biology of the cell at an ever increasing rate.

Figure 2. *High-throughput large-scale sequencing centre. Taken from The Cancer Genome Atlas website. [6] Courtesy: The Broad Institute of MIT and Harvard, the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI). [6]*

Building a roadmap of cancer

In 2006, a joint effort between the National Cancer Institute (NCI) and the National Genome Research Institute (NGRI) in the United States spurred a pilot project called The Cancer Genome Atlas (TCGA), aimed at creating a reference data set of the genomic changes that occur in three major types of cancer. [6,7] This project utilised high-throughput technologies (Figure 2) to sequence and catalogue gene mutations, chromosome rearrangements, gene copy numbers, gene expression profiles and epigenetic changes from collected tissue samples of brain, lung and ovarian cancers. [6,7] This has generated an immense amount of data which is being integrated into an online catalogue, publicly available to researchers around the world. [6]

Mapping the genetic changes in cancer with the integrative analysis of multidimensional genomic data such as DNA copy numbers, gene expressions and DNA methylation aberrations is proving to be extremely informative. In 2008, TCGA researchers identified three major signalling pathways (RB, p53 and RTK/RAS/PI3K) which harboured mutations in 75% of cases of glioblastoma multiforme (GBM), the most common and deadliest form of brain cancer. [12] This suggests that these pathways are promising targets for drug development.

The TCGA database has also contributed to a number of other studies focusing on the genetics of cancer and the list is growing rapidly. [6] One study using data from TCGA identified the gene ANXA7 as a tumour suppressor for the epidermal growth factor receptor gene, EGFR. [13] Mutations of ANXA7 have previously been associated with breast and prostate cancer, whereas EGFR is the most common genetic defect in growth factor signalling in GBM and is implicated in several other cancer types. [13,14] Genetic players such as these, with roles in multiple cancer types, are encouraging targets for the pharmaceutical industry.

In October of 2009, TCGA announced its expansion efforts to characterise over 10,000 tumours from 20 different tumour types by the year 2015, creating a comprehensive database describing the foundations of cancers. [6] This endeavour will significantly increase the rate of advancement for the treatment and management of cancer in tomorrows' clinics. The clinical relevance of understanding the molecular origins of carcinogenesis have already been demonstrated in leukaemia, breast and lung cancer. [2,8] Prognostic tests for specific genetic mutations from tumour biopsies are giving direction regarding which drugs patients will most likely respond to. [7,9,11,14]

Retrospective as well as prospective samples are being collected for TCGA to analyse the changes that occur in the progression of drug resistance, a frequent problem in the treatment of cancer. [6] This will provide insight for the direction of drug development and the future management of the disease. Many patients with GBM initially respond to temozolomide treatment, an alkylating agent, but develop therapeutic resistance which invariably leads to death. [15,16] TCGA data from tumours of GBM patients were analysed before and after treatment with temozolomide for the identification of elements responsible for the development of therapeutic resistance. [16] Mutations in the mismatch repair gene, MSH6, arose after treatment and were found to give rise to a hypermutation phenotype that mediated the resistance of GBM against temozolomide. [16] Eventually, the initially effective treatment developed resistance by selecting for cells with genetic aberrations that enabled the cancer to resist the therapy.

The ammunition: Examples of currently used targeted therapy

Standard cytotoxic chemotherapy does not adequately discriminate between cancerous and normal cells, reducing the efficacy of treatment and increasing side effects. In contrast, targeted therapeutic treatment regimens generally permit the use of higher concentrations for longer durations, with fewer harmful side-effects. Effective therapeutic strategies such as these are already showing promise. Table 1 summarizes several examples of targeted therapies currently in use or being tested. Advances in high-throughput technologies and molecular profiling have also sparked new developments in cancer research, identifying the mechanisms involved in acquired resistance.

Imatinib is a synthetic tyrosine kinase inhibitor used in the treatment of chronic myeloid leukaemia (CML). It is specifically designed to inhibit the BCR-ABL fusion protein which is a result of a chromosome translocation, known as the Philadelphia chromosome. [17] The constitutively active tyrosine kinase targeted by imatinib, BCR-ABL, activates signalling pathways involved in the regulation of bone marrow stroma cell adhesion, cell proliferation and apoptosis. [17] Imatinib has also been shown to block the activity of additional tyrosine kinases, including c-Kit receptor and the platelet-derived growth factor receptor (PDGFR), both of which promote tumour growth. [17,18] Imatinib has significantly increased the effectiveness of CML treatment with fewer complications and side-effects compared to the traditional chemotherapy regimen, with an improved five year survival rate. [17]

Approximately 25% of invasive primary breast cancers exhibit amplification of the receptor tyrosine kinase human epidermal growth factor receptor 2 (HER2). [18] Trastuzumab is a monoclonal antibody which inhibits the activity of the HER2 tyrosine kinase. [19] This targeted monoclonal antibody significantly improved outcomes of patients with HER2-positive breast cancer when used in combination with traditional chemotherapy. [20-22] However, over time the

treatment loses efficacy through the development of resistance, likely mediated through IGF-1 and related EGFR signalling pathways. [19] Pre-clinical studies are currently elucidating the mechanisms regulating trastuzumab resistance for the identification of additional candidate targets for drug development. [19] In addition, another novel antibody, lapatinib, appears to reduce HER2, EGFR and IGF-1 signalling and is showing promise in combination therapy. [19]

The addition of rituximab, an anti-CD20 monoclonal antibody, to the treatment of B-cell non-Hodgkin's lymphoma (NHL) is another example where targeted molecular therapy in combination with standard chemotherapy has become first-line treatment. [11,23] The side-effects associated with rituximab are minimal and have proven to be tolerable for long durations. [11,23] The antibody treatment is now being tested as a long-term maintenance therapy for NHL, and preliminary results from phase III clinical trials have shown that progression-free survival is significantly improved on the maintenance regimen. [24]

The activation of the hedgehog signalling pathway has been implicated in several types of cancer, including basal-cell carcinoma of the skin and medulloblastoma of the brain. [25] The hedgehog pathway is responsible for the control of several processes in embryogenesis and is mostly inactive in adult tissues; thus, blocking this pathway may reveal a large degree of selectivity against the cancer with fewer harmful side-effects. [26] A new compound, GDC-O449, has been found to inhibit the hedgehog signalling pathway and has recently reported to generate beneficial responses in two preliminary studies, a phase I clinical trial and a case report of a patient with refractory medulloblastoma. [25,27] Both studies demonstrated compelling evidence that therapy directed at hedgehog signalling is an encouraging new direction in the treatment of basal-cell carcinoma, medulloblastoma and other cancer types. [25-27] Importantly, molecular profiling of tumours in both studies is helping to characterise the mechanisms involved in hedgehog-regulated carcinogenesis and the development of therapeutic resistance to GDC-0449.

Ligand-independent epidermal growth factor receptor (EGFR) activation occurs in a subset of non-small-cell lung (NSCL) cancer, resulting in constitutive activation of the intracellular tyrosine kinase domain. [14,28] Erlotinib and gefitinib are targeted tyrosine kinase inhibitors of the EGFR that give rise to an improved patient outcome, although not a cure, with modest side effects. [14,18] Mutations in the EGFR tyrosine kinase domain have been demonstrated in a number of other metastatic cancers such as pancreatic, colorectal, breast and glioma, where the efficacy of erlotinib is also being tested. [28]

An exciting new development in the area of gene expression is the discovery of so-called microRNAs (miRNAs). These short regulatory RNA molecules function in the control of gene expression. Microarray analyses of tumours are revealing increasing evidence that these microRNAs also play a functional role in cancer as oncogenes and tumour suppressor genes. [29-31] Studies are elucidating which are key players, and a new class of anticancer therapeutics under investigation is aimed at regulating these microRNAs. [29-31] Theoretically, all RNA or protein molecules that are cancer targets can be down-regulated through a process called RNA interference. This requires the synthetic production of sequence-specific siRNAs which specifically target the molecule in question. Although effective delivery of siRNAs is likely to be the most challenging hurdle in the effective use of RNAi therapeutics, novel strategies exploiting lipid complexes, viral capsids and antibodies may prove to be successful in overcoming these obstacles. [29,32]

Tomorrow's promise

The most troublesome attribute of cancer is its ability to develop resistance against traditional and new age classes of drugs. This is primarily done by manipulating the network of interacting signalling pathways that mediate growth, replication, survival and apoptosis. Past lessons have taught us that monotherapeutic approaches will likely continue to fail in this comprehensive cross-talk model of correlated genes interacting with related signalling pathways. [33] Yet a great sense of optimism remains, as current and prospective technological advances continue to expand our understanding of the mechanisms that drive cancer. The progression towards drug resistance is an evolutionary process of selection, familiar to the field of medicine. However, past successful approaches preventing nature's propensity to adapt should be emphasised, the treatment of HIV being one example. The 'cocktail' regimen of antiretroviral therapy uses several medications which target a combination of biological processes essential for HIV replication, and has been successful in preventing mutations in the virus which regulate drug resistance. The further development of novel therapeutic approaches targeting additional specific mechanisms in cancer will hopefully provide tomorrow's clinicians with a 'cocktail' arsenal of ammunition, capable of surmounting cancer's tendency to adapt.

Acknowledgments

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Table 1. *Examples of some targeted therapeutic drugs currently approved for use or being tested.*

Cancer Type	Drug(s) currently approved or being tested	Drug type	Drug target	Comments
Chronic myeloid leukaemia	Imatinib	Synthetic tyrosine kinase inhibitor	BCR-ABL fusion protein	May also block other tumour-promoting receptors (e.g. c-KIT, PDGFR)
Breast (HER2-positive)	Trastuzumab	Monoclonal antibody	HER2 tyrosine kinase	Resistance possibly mediated through IGF-1 signalling
	Lapatinib	Monoclonal antibody	HER2 & EGFR tyrosine kinases	May also block IGF-1 signalling (implicated in tumour growth and resistance)
B-cell non-Hodgkin's lymphoma	Rituximab	Monoclonal antibody	CD20	Likely mediated through antibody-dependent cell-mediated cytotoxicity, complement and apoptosis
Medulloblastoma	Compound GDC-0449	Synthetic ligand inhibitor	Hedgehog signalling	Hedgehog signalling is implicated in basal-cell carcinoma, medulloblastoma and possibly others
Non-small-cell lung cancer	Erlotinib Gefitinib	Synthetic tyrosine kinase inhibitorSynthetic tyrosine kinase inhibitor	EGFR tyrosine kinase EGFR tyrosine kinase	EGFR mutations are also implicated in other metastatic cancers (e.g. pancreatic, colorectal, breast and glioma)

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Conflict of Interest

None declared.

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Glossary of Terms

Epigenetic processes are changes in the regulation of the expression of gene activity without alteration of genetic structure.

Molecular profiling studies utilise measurement of global mRNA and protein patterns towards identification of individual genes and groups of genes that mediate particular aspects of cellular physiology and pathology. Proteomics is the global analysis of cellular proteins.

Proteomics uses a combination of sophisticated techniques including two-dimensional (2D) gel electrophoresis, image analysis, mass spectrometry, amino acid sequencing, and bio-informatics to resolve comprehensively, to quantify, and to characterize proteins. The application of proteomics provides major opportunities to elucidate disease mechanisms and to identify new diagnostic markers and therapeutic targets.

Metabolomics is the study of the biological metabolic profile of a cellular specimen in a specific environment at an isolated time point. This discipline depicts the physiological states of cells and organisms by focusing on carbohydrates, lipids, and other metabolites. Several analytical techniques are utilized to quantify the metabolic content of specimens such as mass spectrometry and electrophoretic applications.

miRNA or *MicroRNA* is a sequence of single-stranded RNA which is typically 20-25 nucleotides in length and may regulate the expression of other genes. *mi*RNAs are regulatory RNA molecules which are transcribed from DNA, but are not translated into proteins.

RNAi or *RNA Interference* is sequence-specific posttranscriptional gene silencing. It is mediated by 21- and 22-nucleotide small interfering RNAs (siRNAs).

siRNA or *Small Interfering RNA* is 21- and 22-nucleotide double-stranded RNAs. These are the mediators of a sequence-specific messenger RNA degradation process known as RNA interference. *siRNAs* can also be synthetically produced.

Definitions are in part adapted from the National Cancer Institute (NCI) Terminology Browser (http://nciterms.nci.nih.gov/NCIBrowser/Dictionary.do) using the NCI Thesaurus terminology.

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An overview of respiratory disease in Indigenous communities: A comparison to the wider Australian population

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Aim: The objective of this article is to compare the differences in long term health outcomes between Indigenous and non-Indigenous populations with respect to respiratory disease. In order to gain a deeper understanding of the knowledge presented regarding differences in Indigenous and non-Indigenous health, the epistemological grounds for the study will be considered. **Methods:** A literature review was conducted. The data for this review was assembled through searching Medline, Informit, PubMed and the Indigenous Healthinfonet for English language peer- reviewed publications containing the keywords: respiratory disease, Indigenous, rural and Queensland. Thirty-two documents were selected. **Results:** Respiratory disease is distributed disproportionately and occurs with peculiar frequency among Indigenous Australians. Key health indicators such as the disability adjusted life year highlight the inequality between Indigenous and non-Indigenous Australians in terms of health outcomes, although to a much lesser extent than in the past. **Conclusions:** An innovative approach to public health has seen Indigenous communities become more actively engaged in medical care. Of particular note is the increasing frequency with which Indigenous health workers are being integrated into rural practice to follow up patients and bridge cultural and societal gaps. Environmental antecedents are important contributors to health which may be responsible for the high burden of disease seen in many Indigenous communities. These challenges must be addressed as part of a new public health drive to bring health equality to all Australians.

Introduction

Closing the gap between Indigenous and non-Indigenous populations has been a major long-term challenge for many developed countries. [3] In many basic areas such as health, socioeconomic status [4] and education, Indigenous people are left behind. Australia's Indigenous population continues to face a high burden of disease. Many recognised health indicators (such as Quality/Disability Adjusted Life Years) corroborate the severe disadvantage faced by Indigenous Australians when compared with the wider community. [56] In many Indigenous communities respiratory disease is a major cause of morbidity and mortality, particularly in infants and children born into rural and remote Aboriginal communities. [7]

What is respiratory disease?

In order to accurately examine the effects of respiratory disease, it is necessary to define the scope and limits of the group of diseases collectively known to affect the respiratory system. The World Health Organisation defines respiratory tract diseases as those which affect air passages ranging from acute to chronic infections, with common examples being pneumonia and asthma respectively. [8]

The prevalence of acute lower respiratory infections (ALRIs) in Australian Indigenous populations mirrors levels seen in developing countries and are a major cause of hospitalisation among young children. [9-11] Consequently, ALRIs are a leading cause of childhood mortality and morbidity, and place a considerable cost and time burden on carers and medical professionals. [9,12]

In recent decades, population-based studies have focused on intriguing temporal trends affecting Indigenous and non-Indigenous populations

and rates of respiratory disease. It was observed that between 1992 and 2000 the rates of hospitalisation for bronchiolitis in infants (those aged <12 months) were 10% greater in non-Indigenous children when compared to their Indigenous counterparts. [9]

Environmental antecedents were identified by several studies [5-7,9] as a likely causative factor in the high prevalence of respiratory disease in Aboriginal communities. It was noted that Indigenous children commonly show higher rates of purulent nasal and aural discharge [13] in addition to dense colonisation of nasopharyngeal passages with common respiratory pathogens. [13,14] Moore *et al.* [9] offer explanations for observed changes in respiratory disease incidence and hospitalisation rates, which include:

1. Increasing day-care attendance rates. Identified as a clear risk factor for respiratory disease transmission [15] and an important explanatory factor for the increased respiratory disease in non-Indigenous children, as Indigenous children do not use day care facilities to the same extent. [16]

2. Introduction of Haemophilus influenzae Type B (Hib) immunisation in 1993. This has seen a marked concurrent decline in pneumonia hospital admissions. Prior to widespread vaccination, pneumonia accounted for 43% of HiB infection in Indigenous children compared to 7% in non-Indigenous children. [9]

3. Introduction of diagnostic assays which rapidly detect common viral agents responsible for ALRIs. Diagnostic assays allow the rapid identification of viruses such as respiratory syncytial virus (RSV), the leading cause of influenza and bronchitis. Appropriate treatment regimes can be subsequently implemented, thus reducing disease severity. [17]

4. Better management of asthma outside of hospital in primary care facilities. [18] The success of primary health care can in some part be attributed to the high levels of community nvolvement in the practice. Recent changes in the approach to public health have seen Aboriginal health workers become more involved in medical care. Currently, they comprise 65% of the health workforce in Indigenous communities. [19]

The heavy bacterial colonisation rates of young children in Indigenous communities is commonly cited as one of the ramifications of high density living characteristic of many communities, due to a lack of housing. [6] These living arrangements may not be simply due to housing shortages but also from the cultural tradition of centralised

extended family groups living together. The introduction of permanent settlements and contemporary Western-style housing may have altered the context of this cultural practice and many studies have found an increasing risk of lower respiratory tract infections to correlate with the increasing density of living. [12]

Common respiratory diseases

Indigenous Australians are affected by many common respiratory diseases and in order to evaluate and compare the associated health challenges, this discussion will focus on major diseases including asthma and acute lower respiratory infections.

Asthma is a chronic lung disease characterised by a severe immune allergic response. [12] This inflammatory condition is one of the two most common causes of hospitalisation for Indigenous Australians, second only to renal dialysis. In addition, asthma is the second most common self-reported long-term illness among Indigenous Australians. Mortality rates due to asthma among Indigenous Australians are 3.2 times that of other Australians. [35]

Typical reactions cause bronchoconstriction and difficulty breathing. [20,21] Vitalis *et al.* [22] confirmed latent adenovirus-5 infection (causing bronchiolitis or pneumonia) increased the inflammatory cell response in an acute exposure to cigarette smoke in animal models. The resultant activation of CD8+ T-cells in response to ADV-5 causes pulmonary damage, as demonstrated by O'Shaughnessy *et al.* [23] Furthermore, investigations by Fryer indicated that viral infections can reduce M2 muscarinic receptor numbers in the airways, thereby increasing vagally-mediated bronchoconstriction. [25] In the opinion of several authors, it is clear that viral infection may be a predisposing factor for respiratory disease.

Levels of lung function are measured by spirometry, with key measures including forced expiratory volume (FEV) and forced vital capacity (FVC). [4] FEV/FVC ratios are typically lower in Indigenous people than in those of European descent. [7] Musk *et al.* [7] found FEV levels 20% lower than predicted even for asymptomatic patients when conducting a survey of respiratory health in the tropical Kimberley regions of northern Australia. Concurrently, a cross sectional study in Norway [26] found the level of serum RSV antibodies was associated with reduced FEV. It is therefore possible to relate repeated infection with common respiratory pathogens to a cumulative and detrimental effect on airway function, or increased susceptibility to other agents such as tobacco smoke. [26]

Burden of disease

The impact of respiratory disease (and the impact of other illnesses) on Indigenous communities is represented by an aggregate concept known as the burden of disease. The most extensive levels of fatal disease and injury among Indigenous Australians are reported in the Northern Territory Aboriginal population. Overall, respiratory tract infections were a prominent cause of hospitalisation and 50% of infants presented an average of two to three times a month within the first year of life, indicating a higher than average disease burden amongst the population. [27] Generally, Indigenous people suffer a rate of burden of disease approximately 2.5 times greater than the non-Indigenous population. [5] An important measure used by the World Health Organisation to standardize and compare the burden of disease between population groups is the Disability-Adjusted Life Year (DALY). [5] The DALY is a time-based measure of health status used to summarise the burden of premature mortality and disability. [28] The DALY is regularly used interchangeably with a similar measure known as the QALY, or Quality-Adjusted Life Year. [29] In this review it is more accurate to apply the DALY, as it combines the years of life lost due to premature mortality and years of life lost due to disability in summarising the overall disease burden. [5]

The Aboriginal population of the Northern Territory was found to be over-represented in total DALYs, accounting for 47.4% while only consisting 29% of the population. [28] Comparisons with the national average show that the NT has higher proportions of DALYs attributable to acute respiratory infection. [9]

In performing a comparison study based on epidemiological data available from Australian State and Territory Health Departments, Zhao *et al.* [30] explored the discrepancy between health outcomes in Aboriginal and non-Aboriginal people. Much of the difference is said to be attributable to diseases with preventable and environmental antecedents. [31] However, although it was noted that gender differences are apparent in Indigenous respiratory disease mortality ratios, Zhao *et al.* [30] agree with previous studies [3,6,7] that the greater contributing factors to Indigenous health status include diet, lifestyle, education and physical activity, all of which are responsive to intervention. [31,32]

Although rarely recognised, information on the burden of disease and injury in Aboriginal populations comes mostly from comparative studies correlating Indigenous populations with the prevalence of infectious disease and lifestyle disorders. [30,33,34] As such, literature describing the burden of disease is incomplete. This is not necessarily due to lack of interest or endeavour in the field. The extraordinarily low population densities in remote and rural areas make it difficult to 'catch everyone' and correctly record the relevant information.

Epistemological grounds and data collection issues for study

In gaining a deeper understanding and appreciation of the data presented in the literature regarding Indigenous health, it is critical to be mindful of the scope and limitations of knowledge. When approaching public health policy development, it is necessary to engage studies providing quantifiable measures of efficacy and financial cost/benefit analysis. [29] In addition to purely quantifiable instruments, a key element in the success of Indigenous health policy is found by understanding the many interposing qualitative vectors operating in a particular community.

The West Australian Data Linkage System (WADLS) was used in the investigation of the prevalence and changing trends in respiratory disease among Indigenous and non-Indigenous populations. In the context of the population-based study performed, the data available through WADLS presented strong evidence for a change in the prevalence of respiratory disease. However, potential changes in clinical interpretations of symptoms over time could lead to bias or inaccuracy in the study. To avoid this possibility, the study recommends increasing the resolution of ALRI data by desegregation of this categorical term (respiratory disease) into specific pathologies. When ALRI data is categorized by diagnosis, it is easier to avoid sweeping clinical interpretations which may misrepresent the true situation. [9]

Conclusion

Respiratory disease is one of the major causes of morbidity and mortality among Australia's Indigenous people. [7] Population-based studies have demonstrated the higher prevalence of asthma, bronchiectasis and pneumonia among Aboriginal children even in urban environments where access to primary healthcare is significantly improved. [12]

At present, literature on the subject of Indigenous respiratory health is somewhat insufficient in scope and specificity. Although statistics and quantitative instruments are significant in evaluating financial impacts, Indigenous health policy is influenced to a far greater extent by qualitative measures. [29] Focusing on consultative dialogue and furthering policy-makers' understanding of Indigenous health behaviours, beliefs and expectations will continue to see improvements in health and mutual cooperation.

Future research efforts should focus on underlying cultural and traditional input into healthcare in indigenous communities.

Despite a lack of quality research relating to Indigenous respiratory disease, there are many environmental antecedents which can be

improved. Bridging the gap in all areas of disadvantage in Indigenous populations will continue to be an on-going challenge for authorities around Australia. [7]

Conflicts of Interest

None declared.

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Complementary and alternative medicine use among children with asthma in Australia

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Aim: To explore current complementary and alternative medicine (CAM) use by children with asthma in Australia. **Methods:** The results of an audit of CAM use by one of the authors (AMD) in 212 parents of children with a history of asthma, recruited from three different settings (outpatient clinic at a tertiary paediatric hospital, metropolitan and rural practices) were compared to three published studies of CAM use in children with asthma in Australia, as identified by literature review. **Results:** The prevalence of CAM use amongst children with asthma in Australia is 45-61%. Common CAM modalities used include chiropractic methods, vitamins and minerals, homeopathy/naturopathy, spiritual/psychological modalities and diet therapy. CAM was used more commonly in female children and those with persistent asthma, poor control of symptoms or using high doses of medication. Importantly, only a small number of parents report their child's CAM use to their doctors. **Conclusion:** Recent surveys of CAM use among children with asthma in Australia demonstrate a high prevalence which has important implications for those managing paediatric asthma.

Introduction

The current approach to asthma management aims to empower patients with confidence, skills and motivation to manage their asthma. [1] This asthma self-management education approach has seen positive results in asthma health status and markedly reduced unplanned visits. [2] However, it has been suggested that the autonomy given to asthma patients may encourage them to seek a wider range of management approaches and view conventional medical treatments as one of several alternatives available. [3]

Complementary and alternative medicine (CAM) has received considerable attention and popularity over the years. A 2005 Australian population-based survey estimated an overall CAM use of 68.9% with $1.86 billion spent on CAM products in a 12-month period. [4] In a survey of general practitioners (GPs) in Perth, [5] 90.2% of GPs reported being approached to give advice on complementary therapies (CT) and 37.6% were currently practicing CT in addition to conventional medicine.

For the purpose of this review, we will assume that the terms CAM and CT are synonymous and adopt the term CAM for consistency. Although various definitions exist, CAM is commonly referred to as a wide range of medical and healthcare systems, practices and products that are not currently considered to be part of conventional medicine.

[6] However, developing a universal definition for CAM has remained a challenge as different cultures have their own sets of traditional beliefs and what is considered as CAM in one country may be regarded as part of standard treatment in another. [7] CAM may be used as a supplement to conventional treatment or as an alternative (that is, replacing conventional therapies). Publications on the use of CAM among paediatric patients in Australia are limited, but there have been reports in chronic, disabling conditions including cancer, [8] juvenile arthritis [9] and asthma. [3,10,11]

The aim of this review is:

1. To compare the results of an audit performed by one of our authors (AMD) on CAM use in paediatric asthma with other surveys on the prevalence of CAM use among children with asthma in Australia identified on a literature search.
2. To describe the characteristics of CAM users in these surveys.

Methods

Audit of CAM use in children with asthma

One of the authors (AMD) performed an audit of CAM use in children with asthma over a 12 month period. The audit involved recruitment of parents of children with a history of asthma, aged between one and twelve years from three different settings: the asthma clinic of a tertiary paediatric hospital (The Children's Hospital at Westmead (CHW), NSW) (n=84); general and specialist practices in the metropolitan area surrounding the hospital (n=69); and general and specialist practices in rural regions of Bathurst, Orange and Forbes (n=59). Parents of children

under 12 months of age were not included because of the difficulty with diagnosis of asthma in this age range. In addition, parents of children over the age of 12 were excluded because it was felt they may have a different approach to the use of CAM. None of the children had co-existing lung diseases such as bronchopulmonary dysplasia or cystic fibrosis. Those with other non-pulmonary disabilities were included.

A questionnaire consisting of four sections was used in the study:

1. asthma severity (using the Functional Asthma Severity Index); [12]
2. CAM use (a modified version of the questionnaire used in Andrews *et al.* [3]);
3. asthma knowledge of parents (a validated questionnaire); [13] and
4. sociodemographic data.

The study was approved by the CHW Ethics Committee Ethics and informed consent was obtained from parents who agreed to participate in the study. Parents completed the questionnaire either whilst waiting for their child's appointment or were able to complete the study at home and return in a reply-paid, pre-addressed envelope.

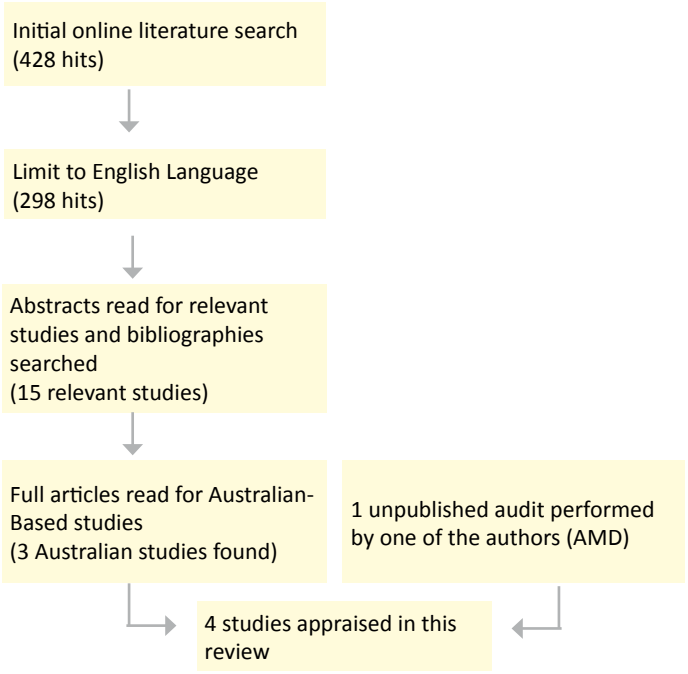

Figure 1. *Flow diagram of literature search*

Literature Search Strategy

Online literature searches were conducted to identify English language articles. Medline, Cochrane and PubMed databases were searched from their inception to 31 July 2009. The search terms used included: complementary medicine or complementary therapies; alternative medicine; asthma or asthma, exercise-induced; child or children. When the keywords used mapped to subject headings, these headings were 'exploded' to include all terms from the hierarchy of controlled index terms. In addition, the bibliographies of articles were searched for further relevant publications. Papers were selected by one author (KH) and were included if the papers were expressed in a way that described general use and incidence of CAM use in children with asthma (that is studies relating to specific CAM modalities and/or their efficacy were excluded) (Figure 1).

There were fifteen studies which fitted our inclusion criteria. These were then reviewed to only include those studies which were conducted in Australia. In total, three studies were found and reviewed and the results compared to our audit. The quality of those articles selected was not appraised in light of the small number of available studies.

Results

Who has been surveyed and how?

The results of our audit and the three other published studies are summarised in Table 1. The previously published studies were conducted in South Australia, [3] Queensland [10] and New South Wales. [11] Sample size ranged from 51-238 children with an age range from 0.7-18.8 years. Subjects were recruited from hospital in-/out-patient admissions and clinics, [3,10,11] paediatric emergency departments, specialist appointments and general practices. [11] All studies adopted a questionnaire method but different styles of data collection were employed. These included face-to-face interviews, [10,11] telephone interviews [10,11] and self-completion surveys. [3] A general exclusion criterion was an insufficient fluency and/or command of English.

What proportion of children with asthma use CAM?

The prevalence of CAM use amongst children with asthma in Australia ranged from 45-61% (Table 1). We found 56% of users were currently still employing CAM, while 44% were previous users. Amongst users, approximately half used only one modality at any one time, whilst a small number used several different therapies. [3] We found that some families reported having tried up to nineteen different therapies. We also found little variation in the use of CAM between city and rural locations.

What is being used?

The common CAM modalities used are listed in Table 2. The most frequently used modalities include chiropractic methods, vitamins

Table 1*. Summary of studies included in review.*

	Donnelly *et al.*, 1985[11]	**Andrews *et al.*, 1998[3]**	**Shenfield *et al.*, 2002[12]**	**CHW Audit, 1999**
Location of Study(city, state)	Brisbane, QLD	Adelaide, SA	Sydney, NSW	NSW
Age Range(years)	-	1-6	0.7-18.8	1-12
Recruitment strategy	Families of children admitted to hospital with either asthma (group A) or minor surgical complaints (group non-A); non-A group had no family members with asthma	Parents of children attending pulmonary Outpatient Clinic or General Medical Outpatient Clinic	Patients with known asthma from Paediatric Emergency Department, Paediatric/Adolescent Wards and private consulting rooms of one investigator	Patients from chest and asthma outpatient clinic, general/specialist practices in metropolitan region surrounding hospital and general/specialist practices in three rural towns
Sample size (survey response)	238:(95.4% A); (91.8% non-A)	51 (93%)	174 (92%)	212
Type of Questionnaire	Interview	Self-completed	Interview/telephone	Self-completed
Prevalence of CAM use	45%	55%	51.7% CM; 24.7% CT	61%

Table 2. *Summary of the most commonly used CAM.*

Study	Most frequently used CAM
Donnelly *et al.* [11]	Chiropractic (21.4%); homeopathy/ naturopathy (18.8%); acupuncture (9.4%); herbal medicines (4.7%).
Andrews *et al.* [3]	Massage (20%); diet therapy (18%); relaxation exercises (16%); positive therapy (16%); meditation (12%); vitamins (12%).
Shenfield *et al.* [12]	*Products*: Vitamins and minerals (53%); herbal preparations (29%); homeopathic remedies (14%). *Therapies*:Homeopathy (32%); naturopathy (32%); Buteyko (11%).
CHW Audit	Diet therapy (45%); vitamins (36%); massage (23%).

and minerals, homeopathy/naturopathy, spiritual/psychological modalities and diet therapy. Shenfield *et al.* investigated the frequency of medicinal CAM use and found that of 145 CAM preparations, 62.1% were in current use, 37.9% had been previously used, 62.8% were used on a daily basis and 6.9% were used several times a week. [11] In most cases, only one modality was used at any one time and half of all preparations were in the form of tablets with the remaining in the form of inhalants, vapours and teas. We found that children from city medical practices were more likely to use faith healing, homeopathy and music therapy than children from other locations (rural and outpatient clinics). We also noted a significant use of Chinese medicine in locations with a greater proportion of children whose primary language was Chinese.

What are the age and gender characteristics of CAM users?
The age of CAM users varied among studies. We found no age relation to CAM use similar to Andrews *et al.* [3] In contrast, Shenfield *et al.* [11] found that children using CAM were significantly older than non-users. However, the age range investigated in that study was considerably different to our study (0.7-18.8years vs. under 12 years). Most studies did not report the gender profile of CAM users but we found female children tended to use CAM more frequently, which is consistent with its use in the general adult and paediatric population. [14-16]

What are the asthma severity and other disability characteristics of CAM users?
We found that persistent asthma, poor to very poor symptom control and higher frequency of doctor visits were significantly associated with the use of CAM which is similar to the findings of Shenfield *et al.* [11] We also noted that children with asthma who have other symptoms or disabilities such as eczema and hayfever, were more likely to use CAM; another finding which has been documented previously. [10,11]

What are the medication use characteristics of CAM users?
Shenfield *et al.* [11] reported that the use of high-dose inhaled or oral corticosteroids and the frequency of side-effects with bronchodilators were related to increased CAM usage. One additional reason cited for the use of CAM was the concern over potential long-term side-effects from corticosteroid use and many parents wanted a 'more natural, less harmful approach.' [11] We only found CAM use to be associated with the use of ipratropium bromide.

What are the characteristics of parents whose child uses CAM?
Although a relationship between higher education and CAM usage has been reported elsewhere, [14-16] we, along with Donnelly *et al.*, [10] did not find any significant correlation. While we found that parents using CAM were more likely to be in paid employment and have higher income, similar to Shenfield *et al.*'s report of an association with parents whose occupations were classified as professional/managerial [11], Andrews *et al.* [3] studied a low-middle occupational status subject population but also reported a fairly high CAM use (55%). Thus, it is unclear whether education, employment and socioeconomic status of parents have any direct influence on CAM usage in children with asthma.

How available are CAM modalities?
It has been suggested that the increasing popularity of CAM is attributed to wide media coverage [10] and increased awareness of treatment options available. [3] Of the paediatric CAM users in Shenfield *et al.*, 33% of remedies were purchased from pharmacies, 23.8% from alternative practitioners, 23.1% from health food shops and 11.6% from supermarkets. [11]

How much are parents spending on CAM?
The costs of CAM use among children with asthma have been found to range from AU$2-$200 per month (medicinal CAM) and AU$25- $400 per month (non-medicinal). [11]

Initiation of CAM use
We found that 83% of CAM usage was initiated by parents/carers after making a personal decision to implement the therapies, 12% were referred by their local doctor and 5% by an alternative healthcare practitioners, with no differences in location of practice.

How satisfied are parents with CAM and conventional medicine?
The degree of satisfaction with CAM in children with asthma has been reported to be between 52.4 – 82.4%. [10,11] When CAM users were asked to evaluate their satisfaction with conventional medicine, 61.2-87.1% were satisfied and 82.8% felt that conventional medicine was effective. [11]

How open are parents about their child's use of CAM?
Shenfield *et al.* [11] found that 47.8% of parents had reported their child's CAM use to their doctors. Typical responses from parents who were not forthcoming about their child's CAM use include 'not worth mentioning,' 'doctors did not ask,' 'irrelevant for doctors to know,' 'doctors are sceptical' and personal choices. [11]

Discussion

A relatively large proportion of children with asthma in Australia have tried some form of CAM with 45–61% of parents reporting the use of CAM in the surveys conducted to date. This is consistent with extrapolated data (50-60%) from a review that examined the use of CAM in adult and paediatric asthma patients. [7]

The common CAM modalities used among the paediatric asthma group have been described in this review. While the list of CAM modalities is extensive and continually changing, it is possible that some CAM modalities were not captured in these surveys. The likely reasons are the use of a pre-determined set of CAM modalities that parents choose from, and many modalities are not being considered as CAM by parents. As mentioned, what constitutes CAM is viewed differently and varies among cultures and beliefs. [7] For example, the most popular forms of CAM modalities used in Turkish children with asthma are quail eggs, herbal medicine, Turkish wild honey, speleotherapy and royal jelly. [17] This implies that a practitioner must be equipped with some information on CAM modalities that are specific to local cultures and beliefs in order to appreciate its implications in management.

What is behind the increasing trend of CAM use? Motivating factors for CAM use can be categorised into 'push' factors from conventional medicine and 'pull' factors from CAM. [18] "Push" factors have been described as 'problematic aspects' of current healthcare that cause parents to look for alternatives. [18] Surveys have revealed asthma severity (persistent asthma), poor to very poor symptom control, higher frequency of visits to the doctor, use of inhaled/oral corticosteroids and the frequency of side-effects of medications are associated with increased CAM usage (push factors). One of the biggest push factors appears to be the use of inhaled/oral corticosteroids and medication side-effects. [11] As children in this category as are usually the more 'difficult' to manage, this presents a dilemma for the practitioner who possess evidence of conventional medical efficacy, but faces parents who do not wish to use these treatments and seek alternatives. Thus,

a practitioner must be equipped with skills of effective communication, empathy towards parents'/patients' requests and the ability to strike a balance between the evidence of science and patient-centre care.

'Pull' factors are described as features of CAM modalities that attract patients into trialling them. [18] Wanting a 'more natural' and 'less harmful' approach [11] are examples described in the surveys. A study in the United Kingdom (UK) [19] found that the benefit of CAM use was the provision of opportunities to explore a wider range of causes of asthma than usually discussed within the normal healthcare system. The study also found that, through holistic treatments, parents were exploring broader questions about their child's health that conventional medicine seemed unable to answer (such as addressing deeper underlying causes of illnesses including social and emotional factors). [19]

Another 'pulling' factor described in the surveys is the wide-spread advertising and availability of CAM modalities. [3,11] Shenfield *et al.* found that 33% of remedies were purchased from pharmacies, 23.8% from alternative practitioners, 23.1% from health food shops and 11.6% from supermarkets. [11] This is consistent with studies [16,20] which suggest that some families were unaware of the difference between conventional medications and CAM, since most supermarkets and retail pharmacies stock CAM products without any clear indication that these products are of a different category to licensed medications. The age of information technology and media [10] has aided the increase in CAM usage and providing 'education' of their presence, effectiveness and availability. Insurance rebates [20] also made CAM affordable to the public through rebates.

From these 'push' and 'pull' factors, it may be implied that parents may be unsatisfied with conventional medicine. However, Shenfield *et al.* [11] and Donnelly *et al.* [10] found otherwise. Despite concerns over the potential long-term side-effects, parents were still satisfied with conventional medications and thought they were effective. Thus, there seemed to be little association between the use of conventional medicines and their effectiveness with the likelihood of CAM use.

One issue that arises from the surveys is patient disclosure of CAM use. Shenfield *et al.* [11] found that 47.8% of parents had reported their use to their doctors, which is slightly higher than reported findings of the general population (20.7% [15] and 37% [16]). A 48% disclosure rate may be insufficient, especially in terms of potential adverse drug interactions and potential harmful substances being used that the practitioner should be aware of in managing their patients. Slader *et al.* [7] suggested several reasons for the varying levels of disclosure in countries where integrative use of CAM has not occurred. These include reluctance to inform practitioners for fear of ridicule, failure of practitioners to directly ask patients and the perception by parents that practitioners would not be interested in knowing. Locally, Shenfield *et al.* [11] found similar responses. This low level of disclosure seems to have both practitioner and parental factors involved.

From a practioner's point of view, it was found that only 28% of CAM use is being documented by doctors with only a slight increase (40%) of use being documented after practitioners are educated about CAM. [21] This may suggest that practitioners are disinterested in CAM or that they do not consider CAM as significant in clinical practice. However, studies of Australian GPs suggested otherwise. Approximately 47% of Perth GPs have undertaken postgraduate studies in CAM [5] and across all studies [5,22,23], 50 – 62.9% of GPs expressed interest in future training. In terms of effectiveness, most GPs in Perth and Victoria saw well-known therapies (acupuncture, meditation, hypnosis, chiropractic methods and yoga) to be moderately to highly effective. [5,24] Thus, it seems that practitioners are quite receptive in integrating CAM with conventional medicine and perhaps, the main problem lies in directly questioning patients on the use of CAM. This was highlighted by Mazur *et al.* [25] who found a 81% increase (from 0%) in reporting rates elicited by direct questioning versus spontaneous reporting by the patient.

From a patient's point of view, studies have suggested that there is a definite perception among the Australian public that doctors are generally disinterested and frequently dismissive and critical of other alternatives. [11,16] In the UK, it was found that a majority of patients felt that health professionals should be more open about CAM and give due consideration and priority to patient's preference of treatment options. [19] Such pre-conceived attitudes about practitioners' acceptance of CAM may add to the pre-existing barriers in many patient-doctor relationships and may contribute to the reportedly low disclosure rates.

The issue with non-disclosure may ultimately be caused by a difference in attitude and perception of practitioners and expectations of parents toward their practitioners. While there are many studies (locally and internationally) which examine the attitudes of practitioners toward patient use of CAM, [26,27] the expectations that parents have of their practitioners have not yet been explored in Australia and knowledge of this may add to improving disclosure and patient-doctor relationships.

Limitations of studies

There are several limitations of the studies reviewed in this paper. Firstly, the exclusion of non-English speaking populations may exclude many CAM users such as recent immigrants who may be more likely to be using CAM. [15] Secondly, sampling of patients from specialist clinics and hospital-related cohorts may not capture CAM users who may not visit their doctors, either because their asthma is well-managed or is not diagnosed. [5] Thirdly, non-disclosure, as discussed, may skew results through reporting bias, as evident in the data of Shenfield *et al.* [11] who conducted home-visits in 10% of their cohort and found that 23.5% of subjects had reported less than actual CAM use. Lastly, self-completed or interview questionnaires may influence results, as experienced in our audit where some subjects may be reluctant to answer the questionnaire fully, resulting in important data being unable to be extracted.

Conclusion

The use of CAM in children with asthma is an important topic that deserves to be drawn to attention. Reported prevalence of CAM use ranges from 45-61% with slightly more than half being current users. Throwing light on this subject will hopefully increase awareness among those managing paediatric asthma.

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Information and support needs of adolescents with Familial Adenomatous Polyposis

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Familial Adenomatous Polyposis (FAP) is a dominantly inherited bowel cancer predisposition syndrome presenting with hundreds of premalignant polyps in the colon. The standard form of treatment is preventative surgery which involves removal of the entire colon. The rectum and colon may also be removed. Predictive testing is usually done at ten to fourteen years of age, and surgery is recommended by the age of 20. Thus, adolescents face a wide variety of difficult decisions and situations. The aim of this review is to critically evaluate existing literature which examines the experiences of these young people and their families, including their information and support needs, psychosocial adjustments and satisfaction with current genetic services.

Introduction

Familial adenomatous polyposis (FAP) is a dominantly inherited colorectal cancer predisposition syndrome which occurs due to the inheritance of germ-line mutations in the APC tumour suppressor gene. [1] It is characterised by the progressive development of hundreds to thousands of adenomas within the colon which, if left untreated, may eventually develop into carcinomas. [2] It is thus imperative that there is early diagnosis and treatment. As the polyps can develop at very early ages, current management calls for annual endoscopic screening, starting at approximately ten years of age. [3]

As FAP is an autosomal dominant disorder with a penetrance of almost 100%, the chance of a child being born from an affected parent is one in two. [4] Therefore, in addition to screening, genetic diagnosis is available from a young age, usually ten to fourteen, and this in itself can result in issues regarding age, autonomy of the child and the desires of parents.

State-based Family Cancer Services are responsible for the provision of genetic testing, as well as subsequent counselling and support following diagnosis. Staff include genetic counsellors, medical geneticists and oncologists who work together to provide patients with information regarding their individual risk, screening options and cancer risk-reduction strategies. [5] Once a diagnosis of FAP is made, patients face complex decisions regarding care, with prophylactic surgery the standard form of treatment. This is a difficult decision to make, particularly for individuals who are otherwise young and healthy, making it challenging to weigh future cancer risks alongside the more immediate impact of surgery. [6]

Such adolescents face a wide variety of difficult decisions and situations. The aim of this review is to critically evaluate existing literature which examines the experiences of these young people and their families, including their information and support needs, psychosocial adjustments and satisfaction with genetic services currently in place. This will provide a greater understanding of the impact such a diagnosis can have, and perhaps lead to the establishment of a variety of age-appropriate services and support.

Methods

Medline and EMBASE databases were used to carry out a search of the literature for English language studies published between 1988 and 2009. The following search terms were used individually and in combination: (Familial Adenomatous Polyposis OR hereditary colorectal cancer OR adenomatous polyposis coli) AND (psychology OR psychosocial aspects OR genetic testing OR genetic counselling OR quality of life OR needs OR support OR information OR surgery). Studies were included if they described empirical research relating to the information and support needs of adolescents diagnosed with FAP, their psychosocial adjustment and satisfaction with current genetic services. Qualitative studies were included due to a limited number of quantitative studies measuring information and support needs of adolescents. Due to the paucity of literature evaluating patient satisfaction with FAP-specific genetic services, studies which evaluated familial cancer clinics regardless of the type of cancer were also considered for the purposes of this review.

Familial adenomatous polyposis: the mucosal surface of the colon is carpeted by numerous polypoid adenomas. (Copyright, UNSW Department of Pathology, from the 'Images of Disease' collection.)

Two hundred and sixty-seven articles were identified through the literature search. Forty-five were retrieved for more detailed evaluation and the final sample included fourteen studies to be reviewed. Reasons for exclusion included articles which did not consider the psychological aspects of FAP, patient cohorts which had been diagnosed with FAP as adults and studies of at-risk patients with a negative test result. Case studies, review articles, conference abstracts and commentaries were also excluded.

Surgery-related impact and needs

The many aspects of FAP mean that deciding when and how it is most suitable to treat patients is difficult and requires careful assessment. The two main forms of surgery are restorative prophylactic proctocolectomy with ileal pouch anal anastomosis (IPAA) or total colectomy with ileorectal anastomosis (IRA).

IPAA involves excision of the entire colon and rectum, leaving the anus and sphincter muscles. A small pouch is fashioned from a loop of the terminal ileum, and an anastomosis is created to attach it directly to the anus. While this heals, a temporary opening in the abdomen, called an ileostomy, is created. This is reversed a few months later, and patients begin to pass normal bowel movements through the anus. [7] In an IRA, the patient's colon is removed and the surgeon leaves 13cm of the rectum which is surgically joined to the small intestine. This is a one-stage operation with a relatively low complication rate, meaning patients generally have normal bowel function afterwards. However, for patients with FAP, there is the persistent risk of developing rectal cancer. [8]

Three papers identified through the literature search looked at the impact surgery has on the psychosocial adjustment of those with FAP. [4,9,10] Notter's study [9] used a purposive sample of women, and conducted semi-structured interviews to assess the main surgery-related impacts on psychosocial adjustment. Findings included distress at the major change brought about by surgery and a feeling of being "disfigured, less feminine, less of a woman"; shock and disgust at the appearance of an ileostomy; and a high level of pain. The study by Osterfield *et al.* [10] used pre- and post-operative interviews to prospectively examine quality of life, personal experience and adjustments in patients who underwent an IPAA. It was reported that prior to having surgery, almost all patients were in good or excellent health and most were afraid of the surgery. Post-operative feelings were similar to those found in Notter's study, with strong feelings of disgust and shame and difficulty adjusting. Severe problems in sex life were a major issue, as was deterioration in work and leisure activities. The findings by Andrews *et al.* [4] echoed those above, with adverse body image, sexual impact and physical functioning being the main factors. Further, all studies suggested that postoperative counselling may improve adjustment to the impact of the surgery, particularly in females.

These studies used three different methods of participant recruitment. That of Andrews *et al.* [4] was a convenience sample, recruited from the Hereditary Bowel Cancer Registries; Notter's [9] was a purposive sample of 50 women, and that of Osterfield *et al.* [10] was a consecutive sample of patients who underwent an IPAA at Heidelberg Medical Centre in a one-year period. All three methods leave room for sample bias, as those who agreed to participate may not be representative of the general community. Despite this, the similarity in findings provides some validity for the conclusions drawn and highlights the important need for careful pre- and post-operative counselling, particularly in the case of young people who may be undergoing surgery at a time when sexuality and sexual functioning is just being established, making it more difficult for them to deal with the issues of body image and sexuality. [9]

Information needs

The need and desire for information about the condition was a consistent theme amongst many studies. [6,11-14] The most preferred source of information was consultation with a medical or genetic expert, [11] and while most patients reported feeling that the professional had provided them with adequate information during a consultation, additional complementary information was often desired. [12] This was most often desired as written material to use as a resource for making a decision about prophylactic surgery.

One worrying aspect of this was the results of a study by Neuman *et al.*, [6] which considered the adequacy of the internet as a resource for making decisions about prophylactic surgery. In this study, a representative internet search was performed which was designed to mirror that of patient searches, and qualitatively assessed the first 50 sites from each search. Of sites identified, 75% failed to include any data relevant to the surgical treatment of FAP, and even those which the researchers considered 'excellent' did not supply details on surgical procedures or postoperative outcomes necessary for decision making. It is possible that the search may be limited due to the simplistic search strategy employed and that more information could be found if a more intensive search strategy was used. However, Neuman *et al.* highlight that this was designed to be a representative sample of available information from a patient's perspective and that it could be easily replicated.

Social support needs

Five studies were identified which documented the impact of social support on the psychological adjustment of persons diagnosed with FAP. Three used self-administered mail-out questionnaires involving itemised rating scales, and one also included open-ended questions. [4,10,14,15] One used semi-structured interviews, [16] and one used a focus group of participants to identify key issues and concerns. [14]

In their study, Esplen *et al.* [14] found that perceived social support was high amongst participants. Scores also indicated a high level of family functioning. However, these two factors were not found to be significantly associated with health-related quality of life. This result contrasts with another study by Osterfield *et al.*, [10] which found that favourable social resources helped the majority of patients to successfully adapt to the challenges and impairments of undergoing surgery for FAP. Similarly, Carlsson *et al.* [15] determined that perceived social support helped to maintain a direct positive effect on mental health-related quality of life for patients with hereditary cancer. It should be noted, however, that the sample surveyed by Esplen used a purposive sample, with very specific characteristics – a diagnosis of both FAP and desmoid tumour, whereas Carlsson *et al.*'s study consisted of a convenience sample and encompassed various types of hereditary cancer, with colorectal cancer being just one form. Thus, it is difficult to directly compare the results of the two studies given the possibility of bias as a results of sampling methods.

However, Carlsson *et al.* concluded that the social support which made the most significant contribution to health-related quality of life was self-esteem and appraisal support - the perceived availability of someone with whom to discuss one's problems. [17] This indicates that it is important for individuals to feel loved, valued and competent. [15] This is supported by Esplen *et al.*'s finding that marital status was a significant and independent predictor for better adjustment, and thus marital status may in fact be a proxy for social support in their study. [14] This finding is also matched by that of Andrews *et al.*, [11] who restricted their study to a FAP affected population and found that being single is associated with higher levels of distress. As FAP is generally diagnosed in early adolescence, it is less likely that these young people will have this form of relationship. This therefore suggests a need to create more age-appropriate resources which may help to provide a further source of support. In response to open ended questions regarding improvements in support services, [11] some adolescents requested support groups be set up locally or on the internet and this is an important possibility to investigate.

Many of these studies however had small sample sizes and several of the sample types accessed may introduce a level of bias. For example, both Esplen *et al.* [14] and Carlsson *et al.* [15] used study groups recruited from clinics, and thus may have been high-functioning, resourceful people not representative of the population. Similarly, the sample of Andrews *et al.* [4] was contacted through the Australian Hereditary Bowel Cancer Register, and those who decline to be on the register may gave different interests to the study group in terms of accessing further social support.

Positive family functioning has also been found to serves as an indicator for better adjustment to FAP. [11,14,16] Duncan *et al.* [16] reported family relationships as being both a positive and negative factor associated with a positive test result for FAP. Patients felt that identifying with other gene-positive family members could be both harmful and beneficial, while others indicated they felt more distanced from particular family members. Esplen *et al.* [14] explain this by reasoning that experience with FAP prior to receiving a diagnosis will only be beneficial if such experiences were positive. If a family member coped poorly with their diagnosis, this will negatively impact the newly diagnosed patient's perception of the illness and their own subsequent adjustment. This suggests that more family-orientated support and counselling may be necessary in the management of FAP for adolescents. This is particularly so given that 77% of one study cohort [11] used family members as an additional source of information and support when they felt that their needs had not been met. It should be noted, however, that Duncan *et al.* [16] interviewed only a small group of people seen at the same genetics service, and Esplen *et al.* [14] used a focus group of seven people to extrapolate some of the aspects of the questionnaire used in their study. Their results may therefore have been biased in that participants may have been those with the greatest

number of concerns.

Satisfaction with current genetic services

Few studies evaluate patient satisfaction with FAP-specific genetic services. Thus, for the purposes of this review, studies which evaluated familial cancer clinics regardless of the type of cancer were considered. Six of the thirteen studies evaluated patient satisfaction with current genetic services and the fulfilment of client needs. [11-13,18-20] However, only four sample sets shall be considered as only four cohorts are described amongst these studies. Further, three of these four samples [12,13,18-20] are based on the one clinic, and thus, an element of bias needs to be considered when analysing the results including the sociodemographic and medical characteristics of those particular participants and service providers. Only the study by Andrews *et al.* [11] involves a slightly broader demographic, having recruited participants from four Australian hereditary bowel cancer registries located in four different states. Bias can still not be ruled out, as those who decline to be a part of the registry may have different opinions to the study group.

The main method of data collection employed was questionnaires. Two study cohorts completed both pre- and post-clinic questionnaires, [12,13,19,20] while the other two completed just one questionnaire post-visit. [11,18] Andrews *et al.* [11] carried out a retrospective study while the others were all prospective. This introduces some bias to the levels of satisfaction participants felt, as the memory would be more vivid for participants in prospective studies. As well, there is a chance for recall bias – patients who have had bad experiences may remember them more than those who had good experiences.

A pilot study on experiences of patients and family members in Amsterdam [18] found that a large majority of respondents were satisfied with the care provided by the geneticist. However, only using a post-clinic questionnaire does not allow for comparison of expectations and participant needs before and after clinic attendance. This issue is more clearly addressed in the studies by Pieterse *et al.* [19,20] and Collins *et al.* [12]

Information needs were generally satisfied in the genetic counselling session. In their study, Collins et. al [12] found that upon arrival at the clinic, most participants wanted 'very detailed' information about each topic; post-clinic, most thought they had received 'enough', and very few indicated that they would need to go back for more. Similarly, Pieterse *et al.* [20] found that the most effective method of communication, in terms of meeting the needs of participants, was the provision of medical information. Clarification of a patient's risk perception helped to ease the worries of some, though it was usually those who were older or less educated. It was thought that perhaps younger people have greater knowledge of genetic concepts and thus a higher expectation of the clinic. [13] For FAP patients, it would therefore be important to ensure that sessions were adapted to suit the information needs of these younger people.

It was further added that additional sessions with a genetic counsellor might be helpful. This was supported by the Andrews *et al.* [11] study, which found that those who had received genetic counselling – on average five years ago, and before the age of twenty-three – could recall only approximately two thirds of the medical and risk information presented, and may not have received information during the consultation for future issues such as childbearing. Thus, there is a need for genetic services which occur on an ongoing basis. The 'before and after' style of data collection used in the design of both Pieterse *et al.*'s [19,20] and Collins *et al.*'s [12] studies may have benefited from a follow-up questionnaire some time after to better assess patient satisfaction with time.

Conclusion

As predictive testing for FAP is usually offered during early adolescence, decisions about surgery and other treatment and management options need to be considered when the patient is very young. Surgical management is highly invasive, making it difficult for otherwise young and healthy individuals to weigh up the future risk of cancer against the more immediate impact of surgery. With few available resources for guidance, patients may be underprepared for the situation.

Poor psychological adaptations are a concern, considering the already documented difficulty in psychosocial adjustment for adults to a FAP diagnosis. [4] The fact that marital status has been found to be a significant and independent predictor for better adjustment [15] creates the question of whether young people, who are less likely to have such a relationship at the time of diagnosis, will be able to find this source of support. While there have been studies in young people which look at their support needs, [4,11] these have been retrospective. This means participants may have had difficulty recalling certain details. It would be useful to ascertain where adolescents feel their main sources of support are, and how this impacts their adjustment to the diagnosis, management and treatment of FAP.

In addition, family functioning has been found to have an impact on the adjustment of adolescents with FAP, particularly when a family member has had a positive or negative experience with the condition. It may be useful to explore the relationships between the affected adolescent and other family members, and whether family-orientated support and counselling may be beneficial.

Considering that diagnosis and surgery for FAP typically occurs in late adolescence or early adulthood, it is disappointing to note that very few papers focus specifically on FAP in a young cohort. Satisfaction with current genetic services has been assessed primarily through studies with a mean participant age of forty. [12,13,19,20] Young people are believed to have greater knowledge of genetic concepts and therefore a higher expectation of clinics, [12] along with a need to focus on future potential issues such as childbearing. Therefore, their experiences of genetic services may differ greatly to that of an older population. This means it is extremely important to determine if adolescents feel their information and support needs are being met in a medical consultation, what additional resources would be of use and whether they feel follow-up sessions would be appropriate, particularly to address post-operative concerns such as impact on sexual functioning and body image.

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What do medical students think about pharmaceutical promotion?

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Aim: The aim of this review was to produce an overview of surveys of medical students' exposure to and attitudes towards pharmaceutical promotion. **Methods:** PubMed was searched for studies featuring surveys of medical students regarding their interactions with pharmaceutical promotion and tabulated the findings for survey questions relating to the main themes. **Results:** Students have significant exposure to promotion, and they generally view receiving gifts as acceptable, but do regard some gifts as more appropriate than others. Most students think pharmaceutical sales representative (PSR) presentations are biased but still of educational value and should not be banned. Most students do not believe promotion will affect their prescribing behaviours. A large majority of students want more education in their curricula on how to interact with PSRs. **Conclusions:** Many medical students think that pharmaceutical promotion is biased and feel underprepared for interactions with the pharmaceutical industry. Despite this, they accept exposure to pharmaceutical promotion believing that it will not influence them. There is scope for improved education in medical schools about this issue.

Introduction

Pharmaceutical promotion in its many forms is a ubiquitous feature of modern medicine. From pens and mugs through to sponsored educational events and conferences, it is estimated each doctor in Australia is exposed to $21,000 worth of pharmaceutical company promotion every year. [1] The scale of pharmaceutical promotion is obvious and its effects on doctors, such as increased non-rational prescribing, increased costs and preferences for newer drugs over older or generic drugs, are well documented. [2,3] Considerably less is known about the interactions between the pharmaceutical industry and medical students. This review will summarise the studies currently available that investigate the exposure of medical students to pharmaceutical promotion and their attitudes towards it.

Criticisms of pharmaceutical promotion are largely focused on its effects on doctors' prescribing behaviour. Since students rarely have a role in prescribing, it may seem that their exposure to promotion should be less of a cause for concern. They are also less likely to discriminate between pharmaceutical companies and it has been demonstrated in one study that most students did not know which company had been responsible for gifts they had received. [4] However, whilst students cannot prescribe and may not draw direct connections between gifts and their source, the behaviour of accepting gifts and the perception of this as acceptable practice may influence their long-term behaviours as doctors. [5] Therefore, any attempts to limit the negative effects of pharmaceutical promotion on doctors must also consider the attitudes and behaviours of medical students. Consequently, this review provides an overview of what is known from surveys about medical students' attitudes and behaviours towards pharmaceutical promotions.

Methods

To find studies that dealt with the issue of medical students attitudes to pharmaceutical promotion, we searched PubMed for English-language papers with the following terms, "attitudes OR survey AND medical students AND (pharmaceutical OR drug) AND (marketing OR advertising)". We did not use "promotion' as a search term because the PubMed definition of advertising includes not only written advertising but also spoken promotion. The main inclusion criterion was that the study featured a survey of medical students on pharmaceutical promotion. Studies were excluded if they did not feature a survey of medical students or could not be accessed in their entirety. The method of analysis was to select main themes that covered most of the survey questions relevant to students' exposure or attitudes to pharmaceutical promotion. An analysis of answers to questions that related to those main themes was tabulated.

Results

The initial search returned 31 papers, of which 17 were excluded as they did not feature a survey of medical students. Another two were excluded as they did not provide enough information about the students' answers or the questions were not relevant to the main themes selected for this review. [6,7] A further three papers were included following a search of the included papers' bibliographies. One study was unable to be accessed in its entirety and was thus excluded. [8] This left fourteen papers in total.

The main themes selected were:

- exposure to forms of promotion;
- perceived appropriateness of gifts;
- bias and perceived value of pharmaceutical promotion;
- whether pharmaceutical promotion should be banned;
- the effects of promotion on prescribing; and,
- education that students receive on the issue.

Key themes addressed in the literature

1. Exposure

Ten of the included studies included questions in the surveys aimed to establish the levels and types of exposure that medical students have to pharmaceutical promotion. All of these studies were performed in North America. All 10 studies found that the majority of medical students questioned had had some exposure to a wide range of pharmaceutical promotion. This included indirect exposure through observations of interactions between physicians and pharmaceutical sales representatives (PSRs) and direct exposure, commonly in the form of personal interactions with PSRs, receiving gifts and attending sponsored events (Table 1).

Table 1. *Levels of exposure to forms of pharmaceutical promotion.*

Form of promotion	Percentage offered and/or accepted (%), by study
Non-educational gift	80 [10]; 91.6 [11]; 94.1 [9]; 95 [12]
Meal (unspecified)- Lunch - Dinner	98.1 [11]; 96.8 [9]; 50.6 [9]; 35 [12]
Book (pocket text or text)	51.0 [9]; 68 [12]; 78.5 [11]
Medical tool (stethoscope etc.)	31 [12]
Frequency of gifts	4.1 / month [9]; 5.5 / year [14]
PSR interactions	80% >1 [10]; 10.6 per month [13]1.2 / year [14]
PSR presentations (at least twice per month)	68 [16]; 17 [17]

Sierles *et al.* [9] found that students in five US medical schools reported an average of 4.1 exposures to any type of pharmaceutical promotion per month. Bellin *et al.* [11] found that 71.7% of clinical students surveyed at the University of Minnesota estimated they had had more than 20 exposures to some form of pharmaceutical promotion. The proportion of clinical students that reported receiving at least one non-educational gift, such as pens or mugs, ranged from 80-95%. [9-12] Students reported varied rates of exposure to PSRs. Fitz *et al.* [10] report that 80% of clinical students had at least one exposure to PSRs over the course of their education at four US medical schools, while students at the Creighton University reported high frequencies of interaction with a mean of 10.6 per month. [13] Canadian psychiatry clerks report attending a mean of 12.2 lunches per year and accepting 5.5 promotional items per year. [14]

Those studies that sampled and differentiated between clinical and pre-clinical medical students found that the percentage of students exposed to promotion and the frequency of accepting it increase with progression through the medical course. [10,11]

2. Appropriateness of gifts

In most surveys, the majority of students indicated they believed that it was acceptable for medical students and physicians to receive gifts from pharmaceutical companies. Sierles *et al.* [9] found that 80.3% of students thought it was, "sometimes okay to accept gifts and lunches because students have considerable debts and minimal income". Fitz *et al.* [10] reported that 65% of clinical students thought that accepting gifts was appropriate and Barfett *et al.* [18] report that 23% of students at a Canadian medical school agreed with the statement that it was unacceptable for physicians to receive gifts. However, in contrast to these surveys, Hyman *et al.* [21] found that only 26% of students at Harvard Medical School considered that accepting gifts was appropriate.

Many students make distinctions as to the level of appropriateness of different gifts (Figure 1). Meals are seen as the most acceptable types of gifts from pharmaceutical companies, with 77.4% of students believing they are appropriate. [9] Students also approve of textbooks as gifts

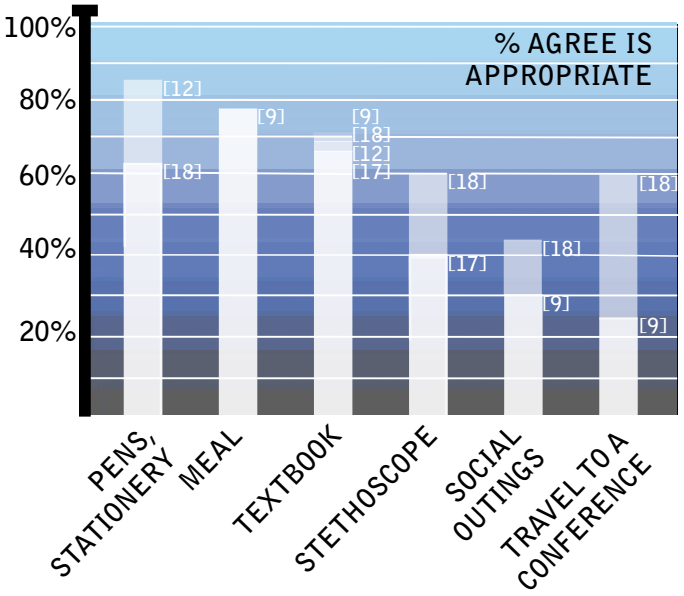

Figure 1. *Student's perceptions of appropriateness of gifts from pharmaceutical companies.*

with 65-71.5 % considering them appropriate. [9,18,19] Stationery (62 % [19] or 4.1 on a 5-point Likert appropriateness scale [13]) and stethoscopes (44-60 % [18, 19]) are also widely accepted, while social outings, drug samples, vacations and funding for travel to conferences tend to be viewed as appropriate by a minority of students. [9,19]

3. Reliability and usefulness of pharmaceutical promotion

Sierles *et al.* [9] found that 67.4 % of students thought grand rounds sponsored by drug companies were biased in favour of the company's product. Monaghan *et al.* [13] asked this question in a slightly different way and found that students gave PSR presentations a mean rating of 2.5 out of 5 for accuracy. Despite this general recognition of bias, many students still value drug company-funded educational sources. [13,14,16,20] Sierles *et al.* [9] found 89% of students thought drug sponsored grand rounds were helpful and educational and 71.3% considered drug company materials a useful way to learn about drugs. Other studies reported smaller proportions of students that shared this view on the value of sponsored events, with 32-46 % agreeing that they had educational value, [14,19] and 22.1% seeing PSR interactions as useful. [20] Outside North America, Ball and Al-Manea [19] found that 60% of students in Kuwait thought promotion was biased and prior to changes in legislation that reduced contact with pharmaceutical promotion, 49% and 45% of Finnish students rated PSR interactions and drug sponsored educational events respectively in their top three most useful sources of information. [16]

4. Whether PSRs should be banned

When asked whether contact with the drug industry whilst in medical school should be limited by banning student interactions with PSRs, most students rejected this proposed action, with 59-82.7% of students in three surveys disagreeing [9,14,18] and a Likert scale rating of 1.6

Table 2. *Perceived effect on prescribing behaviour.*
**Scale from 1 to 5: 1 = strongly disagree, 5 = strongly agree .*

Proposition	Percentage agree (%), by study	Likert scale*
Gifts will have no impact on: 1) my future prescribing 2) my colleagues' prescribing 3) physicians' (in general) prescribing	56 [14]; 68.8 [9]; 57.7 [9]; 72 [10]; 75 [12]	2.8 [13]
Interactions with PSRs will have no impact on my future prescribing	34 [14]	-

(where 1 = strongly disagree) in one medical school. [13]

5. Influence on prescribing

It appears that many medical students feel invulnerable to being influenced by pharmaceutical promotion (Table 2). Of students surveyed, 56-68.8 % believe their own prescribing practices will not be affected by accepting gifts [9,14] and 72-75% of students disagreed when asked more generally if physicians would be affected. [10,12] Sierles *et al.* [9] also demonstrated that students believe that they will be less affected than their peers.

6. Education on this issue

A majority of medical students do not feel adequately prepared by their medical courses on how to interact with PSRs and would like to have more teaching on this included in the course. 61-82.9 % of students felt their medical course did not provide sufficient training [9,21] and 52-77.8 % of students said they would have liked more teaching. [9,16,17] One study found that most students have not even discussed the issue with advisors or instructors. [11]

Discussion

This review has found that studies of medical students' beliefs about pharmaceutical promotion have investigated six main topics: exposure, gifts, perceived reliability and usefulness, whether PSRs should be banned, influence on prescribing and level of education on this issue. Most students had been exposed to pharmaceutical promotion. They tended to believe promotion is often biased and education on the issue is inadequate. Most believed that gifts were acceptable and representatives should not be banned presumably because they believed that promotion was useful.

The widespread belief amongst students that pharmaceutical promotion is often biased is supported by evidence. [22,23] By contrast, student's feelings of invulnerability are contrary to the available evidence that pharmaceutical promotion does influence prescribing. [1-3,5] In addition, students seem to believe that the effects of pharmaceutical advertising will be more pronounced in their colleagues than themselves. This sense of unique invulnerability has been documented previously amongst doctors [3] and may suggest a naïve and inflated sense of objectivity in prescribing, as well as a curious differentiation between their abilities and those of their colleagues.

While students claim pharmaceutical promotion has little effect on prescribing behaviour, they still differentiate levels of appropriateness of gifts, suggesting they do in fact attach some negative value to gifts they view as more expensive, unnecessary or influential (Figure 1). This implies they are at least aware of the negative effects of external influence on their prescribing but assume a "dose-response" relationship between the value of a gift and its potential influence. However, there is evidence to suggest that even small gifts may still have an effect on behaviour. [24] It may also make students more vulnerable to the effects of low value gifts if they do not perceive them to be threats to objectivity or worthy of vigilance. The fact that they see some potential negative effects, even if only from expensive gifts, also suggests that there may be scope for major changes in attitude if they are presented with convincing evidence that pharmaceutical promotion can be effective in misleading them. [12, 25-27]

This review is the first to examine the opinions and attitudes of medical students specifically. Wazana [2] reviewed studies of doctors at all stages whereas Zipkin *et al.* [3] focused on trainees. Their results are similar to ours especially for senior students.

Whilst only intended as a review of the literature available on the topic of students and pharmaceutical promotion, this review nevertheless has certain limitations. The studies that were chosen were only those that were available in English via PubMed, therefore some studies may have been missed. This review is systemic, but is not a quantitative meta-analysis, therefore subjective bias may influence the selection and presentation of information.

All of the studies included in this review had limitations. They used multiple-choice questions or Likert-style questions which may elicit answers that are not indicative of behaviours or attitudes in situ. Students' answers could have been biased by (for example) an inclination to reflect what they believed to be more socially desirable. However, this style of investigation is appropriate to satisfy the aims of each study. [28]

The response rates (when provided) in the reviewed studies ranged from 20-100%, reflecting researchers failure at times to maximise participation by using strategies such as those detailed by Boynton. [28] Particularly in voluntary surveys about ethical issues such as this, studies may crucially overlook those students who choose not to participate. This may be because they have dismissed the issue as unimportant or are apathetic towards it, or indeed are apathetic toward voluntary surveys, thereby potentially skewing the results towards the opinions of those students who have stronger feelings about the issue and hence, participate in the survey.

Selection bias may have occurred in many of the studies. The medical schools chosen may introduce selection bias, as certain schools or locations may imbue students with certain attitudes that are specific to that school, reducing the ability to generalise the results to medical students as a single group. Only five of the studies [9,10,16,17,25] compared responses across different schools with the same instrument, and even then, Sierles *et al.* [9] admit that for their study, schools were chosen non-randomly in an attempt to access a broad sample. In terms of international comparisons, studies undertaken in different countries used different methods, in particular different questions, so the available data is not adequate to determine if there are differences over time or from place to place. If there are such differences further study would be needed to determine if the differences arose from variations in levels or types of pharmaceutical promotion targeting students, as well as students' attitudes or institutional policies.

The implications of this review are chiefly that medical educators should be aware that medical students are exposed to pharmaceutical promotion and, currently, feel underprepared for their present and future interactions with the pharmaceutical industry. Students also tend to have beliefs that appear contradictory to available evidence. This suggests a need to improve medical courses.

To date, there has not been any published research into Australian medical students' attitudes on pharmaceutical promotion. Medical educators in Australian universities would therefore benefit from more information specific to Australian students. Based on this review of previous studies, a study design that would be useful in providing this information should involve a large sample of clinical medical students from multiple universities and a questionnaire that has been validated in previous studies and piloted on a representative sample of Australian medical students. We suggest that the survey used by Sierles *et al.* [9] would be most appropriate and would allow for international comparison.

Conclusions

From this review of the available literature on the issue of medical students' exposure to and attitudes towards pharmaceutical promotion, it is possible to draw the following conclusions. Students have considerable exposure to promotion, and they generally view receiving gifts as acceptable, but do regard some gifts as more appropriate than others. They tend to think PSR presentations are biased but still of educational value and should not be banned. Most students do not believe promotion will affect their prescribing behaviours. A large majority of students want more education in their curricula on how to interact with PSRs.

The issue of pharmaceutical promotion and students should be of concern to Australian medical students and educators, as the evidence from overseas studies suggests students face considerable levels of pharmaceutical promotion without formal instruction on how to best

approach it. It is important to note that none of the papers in this review were based in Australia, so more research in Australian medical schools would be beneficial in order to direct interventions.

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Conflict of interest

None declared.

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'Moore' than just a doorstop: *Clinically Oriented Anatomy* vs. *Gray's Anatomy for Students*

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First Year Medicine (Graduate)
University of Queensland

David recently completed a Medical Science degree at the University of Queensland. As an anatomy demonstrator and an undergraduate representative on the Academic Board, David is heavily involved in education at the university. He carries ambitions for surgical, pathological and anatomical research.

Gareth S Davies
First Year Medicine (Graduate)
University of Queensland

As a recent Bachelor of Science graduate from the University of Queensland, Gareth received the Robert Kennedy Prize in Anatomy in 2007. He has since worked as an anatomy demonstrator in a variety of undergraduate anatomy courses and has a personal interest in anatomical dissection.

Ashwarya Nath
First Year Medicine (Graduate)
Australian National University

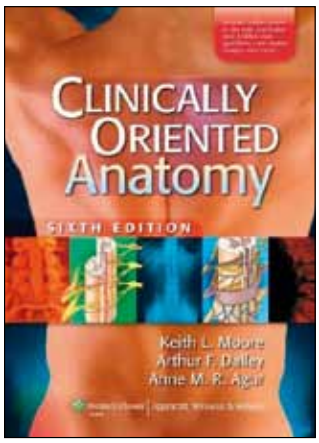
In 2009, Ashwarya graduated from The University of Queensland with a Bachelor of Science (Biomedical and Anatomical Sciences). He has previously held several tutoring positions for first year organic chemistry, human biology and microbiology. He has now made the transition to medicine in Canberra.

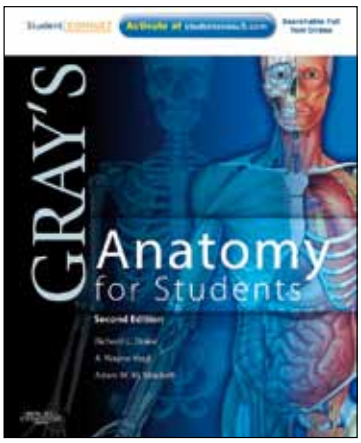
Drake R, Vogl W, Mitchell A. Gray's Anatomy for Students. London: Churchill Livingstone; 2009.

RRP: $138.00

Moore KL, Dalley AF, Agur AMR. Clinically Oriented Anatomy, Sixth Edition. Baltimore: Lippincott Williams & Wilkins; 2009.

RRP: $129.80





The study of anatomy is often a challenging endeavour for many medical students. Central to the learning process is the use of a good textbook. Two of the most often recommended texts for medical students are *Gray's Anatomy for Students (GAS)*, descended from the iconic text by Henry Gray, and *Clinically Oriented Anatomy (COA)*, by Moore, Dalley and Agur.

Both texts employ a regional approach to the study of anatomy. *GAS* separates each chapter into four sections: *Conceptual Overview, Regional Anatomy, Surface Anatomy and Clinical Cases*. The conceptual overview aims to provide the very basic concepts of each region in a concise summary before moving on to an increasingly detailed description. While this approach may be useful for the beginner or reviewer, the inevitable repetition creates a degree of redundancy. *COA* presents information in a 'bones up' format, progressively adding surrounding structures before detailing the arthrology of each region. Each chapter concludes with a series of radiographic images to complement integration and understanding.

Certain striking distinctions are evident in the textual quality of each book. *GAS* aims to strip away irrelevant information into an easy-to-read summation while leaving intricate details for other texts. While this provides an excellent introduction for the neophyte, *COA* includes more rigorous explanations concerning the finer points and the complex interaction with surrounding structures. An enlightening example of the differing styles can be observed through the treatment attributed to the sternocleidomastoid (SCM) muscle. A concise, tabular description of muscular attachments, innervations and basic function is provided in *GAS* in association with a stylised diagram indicating its position in the neck. Conversely, *COA* devotes an entire four page sub-section to a detailed discussion of the manner in which body position and the use of synergist muscle groups can alter function of the SCM beyond an isolated view of the muscle acting independently in the anatomical position. Thus, while simplified to enhance the initial integration of basic concepts, *GAS* may simultaneously perpetuate certain erroneous notions concerning the nature of anatomical function. On the other hand, the text in *COA* may reduce its effectiveness for the uninitiated, while *GAS* may prove to be too simplistic for the interested student.

Both books approach diagrammatical representation through the use of computer-generated imagery, though distinct dissimilarities are visible. *COA* depicts each region by incorporating detailed and realistic diagrams which are thoroughly labelled. In contrast, *GAS* represents analogous images through a distinctly stylised fashion. Major structures are portrayed in an idealistic mode, which, in combination with relatively sparse labelling, may impede practical application, particularly in medical courses focussed on anatomical dissections. However the simplified overview, devoid of extensive detail, is potentially easier to comprehend for the less experienced anatomist. In addition to detailed, accurate labels, *COA* consolidates diagrammatic elements through representations in various anatomical planes. The depiction of distinct layers within each system aids the appreciation of the detailed nature of such structures. Ultimately, *COA* associates these illustrative characteristics through the use of numerous, detailed figures within each specified anatomical region. The use of *COA* may prove to be beneficial, both in dissection and in providing a broader scope of understanding.

The integration of clinical aspects throughout a text is essential to the effective understanding of anatomical information. Both books appear to have achieved a relatively streamlined integration of such information through the utilisation of clinical vignettes. Complemented with relevant diagrams, topics covered in the text of these vignettes include information relating to development, anatomical variation, radiology and pathology. For those without significant exposure to anatomy, having clinical information presented in such a fashion is an ideal mode for the consolidation of vital concepts. The use of end of chapter case studies in *GAS* allows the reader to evaluate their own level of understanding, a feature that is absent in *COA*. Radiological correlations in *GAS* are discussed further through an in-text approach. Alternatively, *COA* utilises radiological imaging juxtaposed with easily understood computer generated diagrams, allowing the student to

understand the concepts therein with more clarity.

Through our experience in both learning and teaching, we believe that *COA* delivers a more comprehensive insight into the study of anatomy. Not only does it encompass a strong clinical foundation, it provides the reader with enhanced factual information and diagrams. Contrastingly, *GAS* offers equivalent aspects in a more concise, readable form yet neglects more in-depth explanations. The choice of textbook will ultimately depend on both the school curriculum and the eagerness of individual students. Whilst providing an excellent synopsis into the anatomical world, the possibility exists that students may find *GAS* lacking after covering the basic concepts. It is our view that *COA* offers greater scope for continued learning throughout medical school and beyond.

Conflicts of Interest

None declared.

Oxford Handbook of Clinical Specialities

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Aniket was the UNSW Medical Society Bookshop Director in 2009. He is in his final year of medicine, and is keenly interested in orthopaedics.

Collier J, Longmore M, Turmezei T, Mafi A. Oxford Handbook of Clinical Specialties. 8th ed. Oxford (UK): Oxford University Press; 2009.

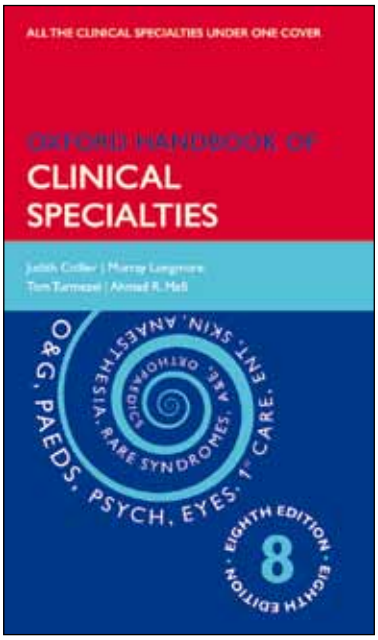
RRP $97.95

As medical students progress through their clinical years, they are exposed to the varied streams of medicine, which not only functions as a key component in their broader medical training, but serves as a degustation for potential specialities they may choose to pursue after medical school. Students often find themselves starting a specialty term without knowing what they need to know, let alone which is the best student-friendly textbook.

The *Oxford Handbook of Clinical Specialties (OHCS)* is divided into twelve chapters, covering streams such as obstetrics and gynaecology, paediatrics, primary care, psychiatry and accident and emergency, which are part of the core teaching in most medical schools. It also covers a number of other important specialities, such as otolaryngology, dermatology, ophthalmology and anaesthetics.

Made as a companion to the *Oxford Handbook of Clinical Medicine* – often referred to as the 'medical student's bible' – this book is another in the *Oxford Handbook* series which provides a solid summary of many clinical streams that will be encountered by medical students as part of general medicine, as well as during speciality rotations.

Like most books in the series, this book is extremely user-friendly. It is divided into different sections based upon fields, with coloured tabs used to help identify each section. Most chapters in the *OHCS* begin with summary pages which deal with the fundamentals of each stream, allowing students to familiarise themselves with the essentials and identify important learning areas. Following this, most chapters spend one or two pages discussing important clinical entities, covering the common, the classical and the critical conditions that medical students should be aware of. Students who have used other Oxford handbooks will be familiar with the structure used to discuss each condition. Where relevant, the book covers the basics – signs and symptoms, investigations, treatment and management, and complications.



Where this book may fail students is in its lack of detail. While the succinct nature of the *OHCS* is useful in the first few clinical years, its brevity also means that the level of knowledge expected of more senior students is lacking. For example, the psychiatry section is an area where this textbook fails to compete with a more comprehensive text. Since psychiatry is a stream that is quite removed from the rest of medicine, the brief summary pages on schizophrenia and affective disorders will doubtless leave students wanting. The dermatology section is also underdone, with not enough space in this pocket-sized textbook to include images of the myriad of integumentary conditions, which is vital for the inexperienced student.

Having said this, the *OHCS* certainly does not purport to be a comprehensive textbook of each of the streams it covers. Tutors will recommend their favourite textbook – the 'must have' for each speciality – which will serve to work biceps as much as brains. Like most Oxford handbooks, the selling point for *OHCS* is that it can fit in one's pocket and is a handy guide to confirm what has already been learned. Overall this is a great textbook for junior-year students entering the clinical environment for the first time, and a useful reference text for senior students.

Conflict of Interest

None declared.

The iPhone: Is it an indispensable tool for medical students?

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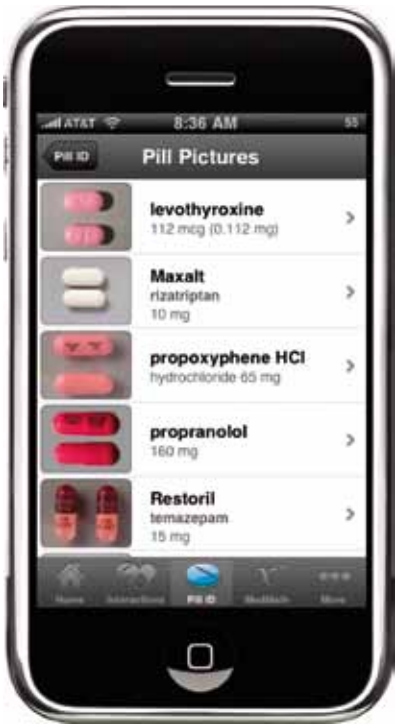
University of New England

Cara is a former nurse now turned medical student. She is the first year representative on the University of New England Medical Student Association.

Technology is always presenting us with new ways of going about our daily lives, and our inability to be separated from our mobile phone, internet or online social networking is growing. Some technology has become obsolete and fallen into obscurity, while some has never caught on. One that definitely has, though, is Apple's iPhone. As medical students, smartphones have the potential to revolutionise our education and training, and one heavy contributor to this is Apple's growing library of medical 'apps' (applications made specifically for iPhones).

'Medical' is a headline category on the iPhone App Store, right next to Utilities, Lifestyle and Games. It is even separate from Healthcare and Fitness – something a good chain bookstore is yet to figure out. Entering this category brings up a multitude of free and paid apps that will be of interest to practicing physicians, medical students or other health care professionals. Finding an app to suit one's needs is made even easier by using one of several online app directories. Apps can do everything from looking up reference values, differentiating between types of arrhythmias to performing useful calculations. While this article cannot hope to delve very far into the thousands of medical apps available, what follows is an overview of some of the most popular ones, which may prove useful for the uninitiated.

The app ABG, or Arterial Blood Gas, can help in the sometimes complicated world of blood gases; simply type in lab values to determine if an acidosis is respiratory or metabolic in nature. Instant ECG (electrocardiogram) displays rhythm strips of many common arrhythmias to study and then provides a quiz to consolidate learning. General Medical History categorically runs through all the questions one should ask to take a medical history. It is very comprehensive, and could be particularly useful for junior medical students who are still becoming familiar with the basics of history-taking. However, pulling out an iPhone in front of a patient, let alone a clinical supervisor, will no doubt fail to convey the best impression.



Some of the big names in textbooks have already made their way to the iPhone platform. The Netter's series of texts is available, including very handy anatomy flashcards. These are an ideal way to brush up on anatomical identification skills while commuting or waiting around. However, some may find that the size of the screen does not do justice to Netter's famous illustrations. The Merck Manual of Diagnosis and Therapy is a guide on the essentials of diagnosis and treatment. Taber's Medical Dictionary is perfect for a mental block on what Klippel-Trenaunay-Weber Syndrome actually is. The original Gray's Anatomy is right amongst the lineup in all its pencil-rendered beauty. However, while it does have a search function, it does not have a table of contents, which is a major oversight. Medscape, Epocrates and Skyscape are bundled apps which include medical calculators and continually updated drug and clinical references – a veritable all-in-one reference for clinicians on the go. Epocrates even has a drug identification tool to allow you to identify a patient's pills.

Table 1. *Prices of popular medical iPhone Apps. All prices are in Australian Dollars unless specified otherwise, and were current at time of publication. All are available from App Store on iPhone or in iTunes, except MIMS Mobile, which is direct from the company. [1]*

App	Price
ABG	Free
Drug Doses	$23.99
EpocratesRx	Free Rx Pro - $99/year Essentials - $159/year Essentials Deluxe- $199/year
General Medical History	Free
Gray's Anatomy Deluxe	$5.99
Instant ECG	$11.90 normally, currently $3.99
MedCalc	Free
Medscape	Free
Merck Manual of Diagnosis and Therapy	$59.99, including 12 months of content updates
MIMS Mobile	US $170 [1]
Netter's Anatomy Flashcards	$47.99
Skyscape	Free
Taber's Medical Dictionary	US $49.95

The Australian-specific content is also increasing. Frank Shann's Drug Doses promises to end the suffering of those who need a little reminder just how many mg/kg of fentanyl to give a child. Likewise, MIMS Australia now has their product available for the platform, allowing healthcare professionals to look up entire product information. Most of the calculator programs such as MedCalc have the ability to change units, allowing the user to easily modify the program to suit the needs of an Australian medico.

One of the drawbacks is that some apps are just not in an affordable price range for many students (Table 1). Netter's Anatomy Flashcards is priced at $47.99, MIMS is an explosive $170, and some, such as Frank Shann's Drug Doses at $23.99, are over double the price of the hardcopy version. However, some of the helpful ones are free, such as Medscape and Skyscape, and there are always useful medical apps on sale. Epocrates has several tiers of its product. The basic version is free, and includes features such as a drug interaction checker and pill identifier. However, to obtain features such as disease images and a medical dictionary, a subscription is required, ranging from US$99 to US$199 depending on the features required.

Another major drawback to some of these apps is that they consume considerable amounts of storage space, such as Gray's Anatomy at 402

megabytes. These larger files also tend to take longer to load. There is also a warranted fear that students may become over-dependent on their phones for answers to questions they encounter on the wards, after becoming accustomed to not having to remember important facts. Students should keep in mind that information will eventually have to come from their heads and not their pockets.

Ultimately, is this all really going to help students with their study, patient care and practice of medicine? It is hard to conclude otherwise. The benefit and convenience of having so many reference texts at one's fingertips, to be able to quiz one's self while waiting for a bus, or to have the ability to easily calculate a PaO_2/FiO_2 ratio at the bedside is undeniable. While students should not start discarding their traditional textbook library, they should definitely start to research or make use of smartphone platforms and their medical capabilities.

Conflict of Interest

None declared.

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[1] Mims Australia. Mims Mobile Pricing [Online] 2010; [1 screen] [cited 2010 Feb 24]; Available from: URL: http://www.mims.com.au/index.php?option=com_content&task=view&id=246&Itemid=267

Nicholas Talley: A career of reinvention

Prof. Nicholas Talley MD, PhD, FACP, FRACP, FRCP
Chair, Department of Internal Medicine, Mayo Clinic Jacksonville
Professor of Medicine and Epidemiology, Mayo Clinic College of Medicine
Consultant, Division of Gastroenterology & Hepatology

Prof. Talley is an Australian-trained clinician and researcher who has been practicing in the United States for many years. In additional to holding the positions listed, he is co-author (along with Simon O'Connor) of the well-known textbook 'Clinical Examination.' In 2010, he will be moving back to Australia to take up a position at the University of Newcastle. The editors of the AMSJ invited him to share his thoughts on his fascinating career-path.

I finished medical school at the University of New South Wales at the end of 1978 wrapping up my course with an inspiring elective at Addenbrookes Hospital in Cambridge, England; they invited me to stay on, but I returned to Australia eager to start my internship, although I had no clear idea of how my career path would progress. I have now been a practicing clinician, researcher and educator for about 30 years; I still love it. Everyone's personal journey is different, and will be influenced by all sorts of external as well as internal forces, some of which are not under one's control. However, we all learn lessons from others and perhaps a few pieces of advice will prove instructive.

Plan to periodically reinvent your career

Re-invention and renewal is the course I have chosen. I spent four years as a resident and medical registrar learning how to become a competent hospital based clinician from 1979 to 1982. I then decided I wanted a break; I was offered a research position with an outstanding academic (Prof. Douglas Piper) and decided to give it a go. I spent three very happy years from 1983 to 1985 undertaking a PhD at Royal North Shore Hospital in Sydney, then a further year as the Professorial Registrar at the hospital, years when I wrote the first editions of my most popular books, as I'll describe later.

I developed a passion for generating new knowledge and publishing it, so I next decided to move to the United States (US) to join an outstanding expatriate Australian (Prof. Sidney Phillips) for further mentorship and training. I expected to stay a year but instead spent seven years in Rochester, Minnesota, initially as a Research Fellow at Mayo Clinic for 18 months and then as a junior faculty member (first as Assistant Professor, then Associate Professor – if you are productive, you can rise very rapidly in the academic ranks in the US).

In 1993, I returned to Australia to take up a new post as Foundation Professor of Medicine at Nepean Hospital, which had just been designated a new Teaching Hospital of the University of Sydney; I was 37 years old, had virtually no administrative experience and was charged with the daunting task of developing teaching and research plus new clinical departments in a hospital that didn't even yet have a physicians training program. I spent nine exciting years developing a fresh dynamic Division of Medicine, introducing the new graduate medical program and actively engaging in research, education and clinical practice.

At the end of 2001 I was offered an opportunity to return to Mayo Clinic in Rochester for a period to pursue a new research passion; I wanted to focus on gene hunting in the functional bowel diseases. As I really knew little about how to do this, I initially undertook a Masters degree in genetic and molecular epidemiology at the University of Newcastle online; I learnt a lot about medical education trends being a virtual student! I had planned to be away about a year, but again was enticed to stay, even though returning to Mayo Clinic in 2002 required me to re-start my research program from scratch once again. I spent four years focused on building my research team and program.

In 2006 I was tapped on the shoulder to become the Chair of the Department of Medicine at Mayo Clinic Florida. My charge was to transform the Department into a cohesive academic entity, and I have

Prof. Nicholas Talley

focused on building teamwork and ensuring financial success while expanding teaching and research. The administrative experience in Florida has been exhilarating; I have learnt more about the science of leading and managing than at any other time in my career. My next (but hopefully not my last) transformation will take place later in 2010; I have decided to move back to Australia to take up the post of Pro Vice Chancellor (Health) at the University of Newcastle, where I will strive to make a positive difference in terms of research and education across the health faculties and in the country.

Strengthen your written and verbal communication skills

Some have asked me how I came to write medical textbooks so early in my career. Frankly, it was the combination of falling upon a good idea, a little luck, and a good team. I saw while having the pleasure of sitting the Fellowship examination for the Royal Australasian College of Physicians (FRACP) that there was an acute need for better guidance on how to prepare for this difficult test. I also recognized many useful clinical examination techniques were poorly discussed in the available textbooks; a detailed systems based approach was largely lacking. At the party celebrating my passing the FRACP exam, I invited Simon O'Connor to join me as a co-author; I knew his wit and style would help add life to the planned manuscript, plus I felt a team would be better equipped to cover the waterfront (and having a co-author

added moral support). I used the extensive card system I had created for the exam to help construct the first textbook. After nine months of working together, we boldly posted copies of the final manuscript to two different publishers, and this is where we had a lucky break; a large publishing house and McLennan & Petty, a small local Australian publishing firm, seemed interested. After discussing the issues with both parties, we decided to go with the local firm; we felt they would give our book their best shot. Examination Medicine turned out to be a surprise hit, and we decided in 1986 while both working as medical registrars at Royal North Shore Hospital in Sydney that we would try writing a bigger and better book for medical students, who we hoped might benefit from the approach we had finally mastered; hence Clinical Examination was born. Many helped us but we had our critics too, especially early on; we were told no one would publish our books, no one would recommend or buy them, and we would offend so many in the establishment that it would limit our careers (some were offended, and we still have our critics). We blissfully ignored the politics and thankfully the critics were largely proved wrong; the books were praised in published reviews and both have now gone through six editions. However, I must be honest; I myself continue to be amazed at the success of the books.

My advice then is to develop your written and verbal communication skills to the highest possible level; take every opportunity to practice public speaking and medical writing! This skill set will stand you in good stead whatever you do in medicine, whether communicating one on one with a patient, presenting to thousands of people in a lecture hall, or writing a book or an article like this one.

TThe Mayo Clinic in Florida. (Copyright, 2010, Mayo Foundation for Medical Education and Research.)

You can make a difference

In this century of rapid change, I suspect it will be more important than ever to be prepared to learn to reinvent yourself. Medical school can lay only the groundwork; much of what you are diligently cramming now will, at best, be seen as quaint in ten to twenty years. You have the chance to transform medicine if you so desire; I am optimistic your generation will boldly grab the opportunities. Becoming an academic was the best decision for me; I hope some of you will be inspired to follow this path. We need leaders who will educate the next generation, create knowledge, and deliver new and better models of clinical care; the job is incredibly rewarding. I wish you every success in your career, wherever it takes you.

What's wrong with the Nobel Prize?

Heather Lee
Fifth Year Doctor of Philosophy (Medicine)
University of New South Wales

Having completed a Bachelor of Science with Honours in Biochemistry at University of Sydney, Heather commenced her PhD studies at the Garvan Institute in 2006. Her research examines Elf5, a gene involved in mammary gland development and breast cancer. On completion of her thesis this year, Heather hopes to continue working in medical research.

Winner of the Co-Op Bookshop Prize for Best Feature Article in this issue of the AMSJ

Introduction

The Nobel Prize is the single greatest honour that can be bestowed upon a scientist, and yet it has received its fair share of criticism. Even Nobel Laureate, Max Dulbrück, has criticised the Prize stating "by some random selection procedure, you pick out a person and make them the object of a personality cult. After all, what does it amount to?" [1] Recently, there have been calls to reform the Nobel Prizes with ten scientists writing an open letter to the executive director of the Nobel Foundation. [2] This article presents a critical analysis of the Nobel Prize and its role in science, showing that whilst flawed the Prize is still valuable.

The origin of the Nobel Prize

The Nobel Prize is named after Alfred Nobel, who made a fortune in the munitions industry after inventing dynamite. When he died in 1896, Nobel's estate was worth more than 33 million kronor with one year's interest from the fortune equal to the annual budget of Sweden's greatest university. [1] Nobel's will, written in 1895, dedicated the majority of this estate to prizes for those who had "conferred the greatest benefit on mankind" by making "the most important discovery or invention" in the fields of physics, chemistry and physiology or medicine. In just one short paragraph, Nobel directed how the Prizes should be awarded: the Swedish Academy of Sciences was appointed to award the Physics and Chemistry Prizes and the Karolinska Institute was given responsibility for the Prize for Physiology or Medicine. [3] Nobel also included Prizes in Literature and Peace, but these will not be discussed in detail in this article. For various reasons, Nobel's will remained in legal peril until 1898 when the Nobel Foundation was finally established as the legal legatee. [4] In 1901, five years after Nobel's death, the first Nobel Prizes were awarded.

The role of the Nobel Prize in recognising and rewarding great discoveries

The purpose which Alfred Nobel intended his Prizes to serve remains their primary role: to recognise and reward great scientific discoveries. [5] Indeed, one of the reasons that the Nobel Science Prizes now demand so much respect is that their histories give testimony to many of science's most significant discoveries. Only on a few occasions has a Nobel Prize in Science been awarded for an undeserving discovery. Most notably, Johannes Fibiger won the 1926 Nobel Prize for Medicine for discovering that parasites caused cancer, a discovery which later turned out to be completely unfounded. [1,6] There have also been instances in which outstanding advances in scientific thinking have gone unrecognised by the Nobel Prize. Alfred Einstein, although awarded a Nobel Prize for the discovery of the photoelectric effect, received no recognition for his most important achievement, the theory of special relativity. On the whole however, the Nobel Prizes for Science have been awarded for great scientific discoveries. The prizes have found their value in the calibre of their recipients. [5]

The Nobel Prizes for Peace, and in particular Literature, have not fared as well. [1,4] In the early years the Nobel Committee for Literature favoured conventional authors and failed to recognise greats such as Tolstoy. Consequently, the reputation of the Literature Prize was damaged and still suffers. Some suggest that the Science Prizes have

enjoyed more success because science is objective, and the selection of Prize winners is less arbitrary than in the subjective fields of literature and peace. This is not the case. The selection process for the science awards is also subjective and may be influenced by the bias of the decision-makers.

Is the decision-making process arbitrary?

The statutes of the Nobel Foundation dictate rules for selecting Prize winners, adding several criteria to those stipulated by Nobel. These can be summarised as follows: [7]

- Prizes may only be awarded for work that "by expert scrutiny has been found to be of ... outstanding importance" and of great benefit to mankind.
- "The awards shall be made for the most recent achievements in the fields of culture referred to in the will and only for older works if their significance has not become apparent until recently."
- "To be eligible to be considered for a Prize, a written work shall have been issued in print or have been published in another form."
- Prizes may not be awarded posthumously but a Prize may still be presented if the Prize winner dies before the presentation ceremony.
- Prizes may be shared between two or three co-workers or between two discoveries but not between more than three people.

The Foundation's statutes also provide guidelines for nominations and adjudication of the awards. Nominations are not open to the public and to be considered for an award, a written nomination must be received from "a person competent to make such a nomination." This includes all Nobel Laureates, members of the Prize-awarding bodies (the Swedish Academy of Sciences and the Karolinska Institute) and those invited to submit nominations. [6] Each Prize-awarding body sends out thousands of invitations every year to scientists world-wide, and a rotation system is used to include as many people as possible. Nominations for an award are then considered by a subset of the Prize-awarding body, the Nobel Committee, which consists of three to five persons appointed by the Prize-awarding body. After careful deliberation, the Nobel Committee votes to determine which candidate should be recommended for the award. Although the final

decision is made by the Prize-awarding body, the recommendation of the Nobel Committee is generally upheld, meaning that the decision effectively lies in the hands of just five people. Since there is no empirical means by which the value of a discovery can be weighed, the Committee members' partialities and understanding of science can easily influence how Prizes are awarded. [8]

In order to protect the decision-makers from criticism and protect the reputation of the award, the Foundation's statutes include a secrecy clause. [9] This states that "no appeals may be made against the decision of a Prize-awarding body" and that "investigations and opinions concerning the award of the Prize may not be divulged." Only after fifty years and for historic research may any records be accessed. Thus, the decision-making process is by no means transparent.

The lack of explicit criteria on which decisions are based, the small number of people responsible for making decisions and the secrecy in which they are made are ample reason for questioning the objectivity of the decision-making process. However, it is difficult to imagine a better system for determining which discoveries are most worthy of the Prize. Opening the award to popular vote (to increase the number of people involved in making the decision) is not a feasible solution given the level of technical understanding and historical research required to make a well-informed decision. Ultimately, whatever the process, there is no objective way to determine which discoveries "have conferred the greatest benefit on mankind." Yet, this is hardly sufficient grounds for abolishing the Prize altogether given that the Nobel Prize serves additional purposes.

The Nobel Prize and its effect on the public profile of science

As well as recognising and rewarding great discoveries, the Nobel Science Prizes serve to boost the public profile and knowledge of scientific endeavours. [10] In a world where media thrives on spectacle, the Nobel Prize ensures that, at least once a year, science is in the spotlight. By raising interest in science, the Prize may also indirectly boost funding for research. The effect that the Prize has on common knowledge of science is less clear. Whilst most people are aware that the Nobel Prize is a great honour for scientists, few would remember last year's recipients let alone what the Prize was awarded for. [1,10] The Nobel Prize no doubt plays a valuable role in boosting the public profile of science, but at the same time has been criticised for presenting a flawed representation of science.

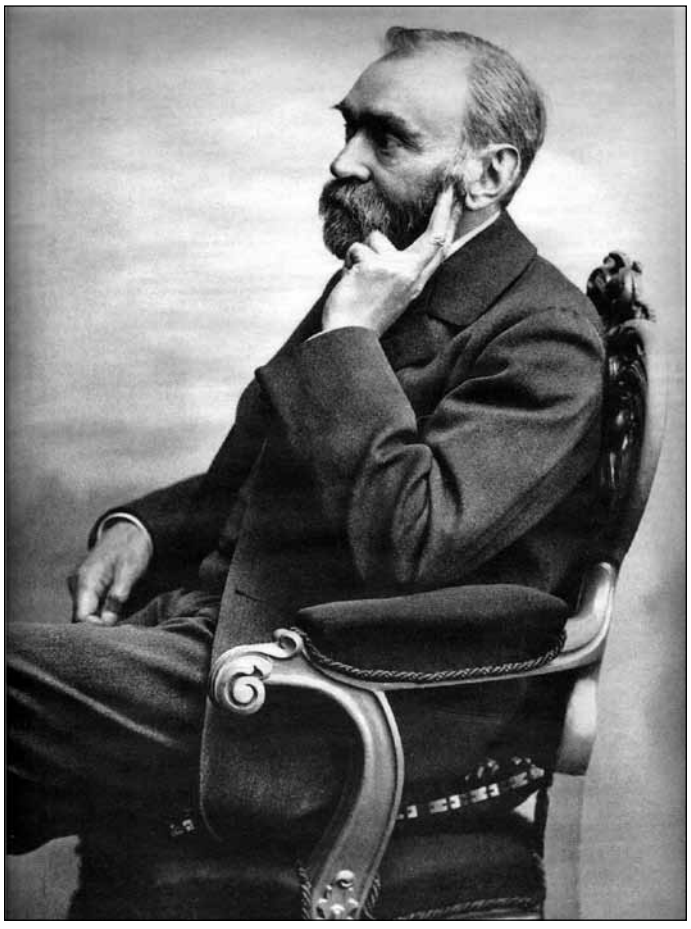
As the world's most prestigious scientific award, the Nobel Prize is often regarded as representative of what constitutes science. However, the disciplines recognised by the Nobel Prize were determined by Alfred Nobel and do not include important fields such as mathematics and biology. In 1968, the then relatively new field of economics managed to capture some of the limelight when the Bank of Sweden 'invented' a Prize in Economic Science in memory of Alfred Nobel. Since then the statutes of the Nobel Foundation have been modified to prevent the formation of any further Nobel awards. Disciplines such as mathematics have established their own awards to contend with the Nobel Prize. The Fields Medal, founded in 1924 by the International Congress of Mathematicians, has grown in popularity but remains overshadowed by the Nobel. It seems unreasonable to deny certain fields of science the recognition afforded by the Nobel Prize simply because Nobel chose not to include them in his will. In excluding some fields, Nobel may have unintentionally affected the public perception and recognition of those areas. This issue was raised in the recent open letter to the Nobel Foundation, with the signatories calling for the formation of two new Nobel Prizes in the areas of global environment and public health and a reform of the Medicine Prize to include all areas of biology. [2] The authors argue that these changes would allow the Nobel Prize to recognise important discoveries in new fields of research that do not fit well into the disciplines specified by Nobel. However, these suggestions were not welcomed by the Nobel Foundation, which maintains that no new prizes will be created. [11]

Recognition of individuals and the co-operative nature of science

Just as the Nobel Prize does not recognise all scientific disciplines, it is incapable of acknowledging all great scientists. Since the Nobel can be shared by no more than three people, a Prize is often awarded to only a few of the scientists involved in making a discovery. [1] Exactly who receives the Nobel Prize is often determined by subjective means and is frequently the cause of disputes and divisions within the scientific community.

An example of this includes the 1923 Nobel Prize for Medicine, long steeped in controversy. [1,12] The Prize, awarded for the discovery of insulin, recognised the work of Frederick Banting and John McLeod, but not that of co-workers Charles Best and J.B. Collip. As the Prize could not be shared by all four researchers, the Nobel Committee was forced to compare the contributions each made to the discovery of insulin. It was under McLeod's supervision and in his laboratory that the discovery was made. [10,13] However Banting refused to acknowledge McLeod as a co-discoverer. After all, it was Banting's idea for a new experiment that had led to the discovery, and McLeod was away in Scotland when Banting and his undergraduate assistant, Best, performed the first critical experiments. Whilst Collip, a biochemist, played an important role in purifying insulin for clinical trials, he was not involved in the initial isolation of the hormone. When Banting heard that he was to share a Nobel Prize with McLeod, he was furious. Persuaded not to reject the Prize, Banting instead acknowledged the work of Best and announced that he would share the cash award with him.

A similar scenario arose in 2003 when the Nobel Prize for Medicine was awarded to Paul Lauterbur and Peter Mansfield for the development of magnetic resonance imaging. Unrecognised was Raymond Damadian, who made the crucial discovery that normal and cancerous tissues have different proton relaxations, and first proposed an external nuclear magnetic resonance scan. [14] Damadian was so outraged



Alfred Nobel

that he placed several full page advertisements in leading American newspapers. [15] Entitled "The shameful wrong that must be righted" the advertisements asked readers to cut out a slip and send it to the Committee demanding that the truth be told. Of course, Damadian's efforts were in vain given that the Foundation's statutes state that "no appeals may be made against the decision of a Prize-awarding body."

The Foundation's exclusion of posthumous awards has also robbed some scientists of well-deserved recognition. For example, the 1962 Medicine Prize was awarded to James Watson, Francis Crick and Maurice Wilkins for their work on the structural propereties of DNA, whilst Rosalind Franklin (who performed critical x-ray crystallography experiments) was not recognised as she died in 1958. Since the fame of the Nobel Prize outlives its recipients, it seems unreasonable to exclude some scientists because they may not live to receive it in person.

Determining exactly who should receive the credit for great scientific discoveries will always be a difficult decision. Although scientific discoveries may have been made by independent individuals in Nobel's time, this is no longer the case. [1] Scientists now work in teams and networks with collaborations, conferences and research centres. [8] We have entered the world of 'big science' where research papers and grant applications are seldom submitted by a single author. Attributing scientific discoveries to individuals now makes as much sense as presenting a gold medal to just one member of an Olympic relay team.

For this reason, the Nobel Prize will always spark controversy and may be considered an anachronism. However, it is also worth considering that the value of the Nobel Prize lies in its exclusive nature, and may depreciate if the statutes were relaxed to recognise the contributions of more scientists.

Conclusions

The Nobel Prize, like any human institution, is flawed. Whilst the Prize has an important role in recognising scientific discoveries, the selection of Prize winners is largely subjective. The Nobel Prize also boosts the public profile of science but may give an inaccurate representation of what science is. Further, recognition of individual scientists seems outdated in the collaborative world of modern science. What then are we to do with the Nobel Prize? Though some may call for abolition, such an extreme measure is no more necessary than it is likely. Is a better model possible? Certainly a Prize allowing for recognition of research groups would be more consistent with the co-operative nature of science, but change is improbable in the well established Nobel Institution. So, we must learn to enjoy the Nobel Prize for what it is worth, remembering that it is not the be all and end all of science, but rather a celebration of some of science's greatest discoveries.

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Applying the retrospectoscope to an elective: Reflecting on six weeks in Timor-Leste

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Throughout Belinda's schooling and medical training, she has been interested in and committed to providing better healthcare for the developing world. She ultimately intends to work in international health, hopefully in a surgical role. She submitted this elective report to the AMSJ as a final year medical student.

The medical elective is notorious for being an excuse for taking a holiday in an exotic corner of the world. Like many of my colleagues, I also travelled to one such corner, Bairo Pite Clinic in Timor-Leste (the official name of East Timor), in search of an adventure with some medical experience thrown in. In retrospect, those six weeks were without doubt the steepest learning curve of my medical training. However, there are a number of things I wish I had known and a great number I would have done differently. Therefore please let me share some insights I have gained with use of the retrospectoscope - the device in medicine which enables the viewer to judge past events or actions with the aid of knowledge obtained since they occurred. This is in the hope of equipping you with some knowledge to make your elective experience the time of your life.

Language

I arrived in Dili, the hot, dusty capital of Timor-Leste after an almost sleepless night in Darwin airport and with a four-word vocabulary of Tetun, the local language. Nevertheless, I was almost immediately loaded onto the clinic's four-wheel drive ambulance to embark on my first of many mobile clinics into the mountains. For such clinics the four-wheel drive is loaded up with a box of very basic medications, and a driver, a doctor or medical student and a medications dispenser drive up to six hours on a road resembling a goat track to a remote village. There, they see a queue of patients – some waiting, some materialising from the surrounding forest- and drive back, often with acutely ill patients. And thus was the experience from which stems my first insight – learn some of the language.

Despite having an 'interpreter' - she spoke as much English as I spoke Tetun - I was luckily armed with the Lonely Planet Tetun phrasebook, which I think saved more lives than I did that morning. Daily Tetun lessons, jotting phrases on the back of my hand and the phrasebook ensured I quickly picked up enough language to hold a reasonable medical consultation. Despite this, I wished countless times I knew some Tetun before I arrived in-country. If you are planning on travelling to a non-English speaking country, do try and learn some local language before you depart. Being able to communicate with your patients makes a world of difference.

Pre-Read

After my mobile clinic baptism of fire, I returned to the Bairo Pite clinic in Dili to be confronted with the afternoon ward round, and a lady in the final stages of labour. Prior to my elective I had seen one patient with tuberculosis (TB) and delivered five babies. Score at the end of the first ward round: 67 TB patients and eight babies delivered. I vividly recall returning to my room that night acutely aware of how much I did not know. I sincerely wished then that I had taken the time to read up on the common problems experienced in Timor: tuberculosis, malaria, labour and its common complications and gastroenteritis. A basic understanding of how to identify and manage these conditions in resource poor countries is essential to getting the most out of your elective. The World Health Organisation (WHO) has some great articles on managing these and other health issues specific to the developing world. [1-4] I thoroughly recommend utilising these prior to and during your elective. Along with the Lonely Planet phrasebook these articles saved a number of lives.

Timorese girls from the Gleno Orphanage, located about 40km or a two hour drive from Dili in the Emera Mountains. The mobile clinic from Bairo Pite Medical Clinic visited the orphanage monthly.

Patients waiting to be seen at a mobile clinic; Bacau, Timor-Leste, 2009 .

Change the World

Before travelling to Timor-Leste, a number of people warned me against thinking I could change the world in six short weeks. And, yes, I completely agree with them, it is not possible. However, do not allow anyone to convince you of the disillusion that you cannot make a difference, but, like chocolate cake, there is a delicate balance between too much and too little. During my time in Timor-Leste, I fluctuated between strategising how to revolutionise their health system and becoming exasperated with the staff, the patients and the system itself.

I only found this happy medium after many discussions with long-serving expatriates, my supervisor, the famous Dr Dan Murphy and a 24 hour flight using the almighty retrospectoscope. Be aware that revolutionising the local health care system includes ensuring nurses actually take observations rather than just filling in normal results; it is amazing how your patient can be saturating at 99% when the clinic does not have a working saturation probe! The work ethic in Timor is much more relaxed than the Australian system, and it is worth remembering that the way you are used to is not necessarily superior and you are the visitor, so embrace and work along with their system. And remember, change on a big scale, if you want it to last, takes time, dedication and education. So if you are planning a revolution, be prepared for your elective to go for six years rather than six weeks.

However, it is also worth noting that you can make a difference for

each patient in each situation. If you do take the plunge and go to a far-flung corner of the globe for your elective, you will more than likely find yourself in a situation where you are the most qualified person available. One approach is to consider the ethical dilemmas raised by such a situation. For example, "Is it ethically responsible for me to treat this patient when they would be under the care of a sub-specialist in Australia?" Alternatively, you can revert to medical and ethical basics: 'air goes in and out, blood goes round and round; and first do no harm.' Application of these principles might just make a difference in the life of a patient and their family, and you might even save a life. It is a bit like the old parable of the starfish on the beach. In the time you have got you cannot make a difference to everyone, but do not forget the opportunity you have to make a difference to that one.

The most vivid experience I had of this conundrum was late one afternoon when a young lady was brought in. Her Glasgow Coma Scale was about 3-4, she was febrile (~41˚C), tachycardic (~150bpm) and hypotensive (70/30 mmHg). She was prostrating and, according to her family, had had three seizures. While the various causes of impaired consciousness from hypoglycaemia to medulloblastoma jumbled through my brain, I quickly looked around for someone, anyone, to help. Alas, at 7pm on a Friday I was left with a local nurse (who helpfully suggested this was most likely cerebral malaria) and the very friendly, but largely unhelpful cleaner.

And thus, I was stuck between a rock and a hard place: if someone did not do something soon this lady would die, and as much as I just wanted to get swallowed up by a hole in the ground, I was the most qualified person in the vicinity. The first priority was her airway, so with shaking hands, in went a Guedel airway, and one of her family members stood with a bag and mask giving her Bi-level Positive Airway Pressure. Bloods were taken and confirmed falciparum malaria with a parasitaemia of about 11%, which is extremely high. Anti-malaria treatment was commenced with Arestunate (as per the WHO guidelines) and within three hours she was sitting up asking for food.

When I talked to my supervisor the next morning he, rather unhelpfully, pointed out that I should get used to feeling out of my depth; it comes with the job. But, the medical education I had received, although not yet technically complete, gave me the ethical responsibility to do what I could for that patient. If you are prepared to travel to a remote medical facility in search of adventure, you also need to be prepared to implement your medical training; you will probably be surprised by how much you actually know.

An arrow in the chest of a young man from one of the mountain villages. The tip of the arrow was lodged in his right atrium

Learn

My supervisor in Timor-Leste, Dr Dan Murphy, is a stickler for learning. If I did not know something, I was expected not only to look up the answer but also read around the topic. If you are like me and learn better under pressure, I highly recommend Bairo Pite Clinic. Dr Dan is a great teacher and will ensure you are a professional at detecting cardiac murmurs and reading blood films by the end of your rotation. He will also encourage you to read about topics, especially any you show a fleeting interest in. So my final enlightenment is go somewhere with good, inspiring supervision. Even with the use of the retrospectoscope, I would not change this element of my time in Timor for the world.

Conclusion

In conclusion, your elective can be an exceptional opportunity for adventure, to learn something and do something productive with your medical education. For those who like a challenge, hot weather and who flourish under pressure, I can thoroughly recommend Bairo Pite Clinic in Timor-Leste as an ideal elective location. And finally, do not be afraid to milk your connections; getting things done in resource poor countries is really all about who you know, not what you know, so please feel free to send me an email for more information or local contacts.

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A very good iDEA: The inaugural gathering of the student division of Doctors for the Environment Australia

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Third Year Medicine (Graduate)
University of Notre Dame (Fremantle)

Elizabeth completed a Science Degree and Masters in Public Health prior to starting Medicine. In 2009, she was the National Student Representative for DEA, an active member in the West Australian Student Environmental Network (WASEN), and a convener of iDEA. This year she is a Publications Officer for DEA students.

Catriona Soutar
Third Year Medicine (Graduate)
University of Sydney

Catriona completed a Bachelor of Arts/Bachelor of Science at the University of New South Wales prior to starting Medicine. In 2009 Catriona was the NSW student representative for the DEA students and she continues this role in 2010.

Imogen Hamel-Green
Third Year Medicine (Graduate)
University of Melbourne

Imogen is a past student union environment officer at the University of Melbourne. In 2009 she was involved in starting the University of Melbourne Green Health Group, as well as being a convener of iDEA, a Victorian State Representative for DEA students and an Australian Youth Climate Coalition (AYCC) representative. She is currently the National Project Officer for DEA students.

Sophie Gascoigne-Cohen
Fourth Year Medicine (Graduate)
University of Melbourne

Sophie completed a Bachelor of Arts (Languages) at the University of Sydney prior to starting Medicine. In 2009 she helped start the University of Melbourne Green Health Group, was a State Representative for DEA students and one of the conveners of iDEA. This year Sophie is the DEA International and NGO Liaison Officer for DEA students.

James Correy
Third Year Medicine (Undergraduate)
University of Tasmania

James is an active member of local grassroots climate action groups in Hobart and has been influential in establishing an eco-health discussion and social group amongst medical students at his university. This year he is one of the two Publications Officers for DEA students.

In early December 2009, just prior to the much-hyped COP15 round of United Nations climate negotiations in Copenhagen, 40 medical students, representing six states and eleven medical schools, descended upon Melbourne for iDEA, the inaugural gathering for the student division of Doctors for the Environment (DEA). Attendees were encouraged to be mindful of their carbon footprints whilst travelling to the conference, with many students opting for train or coach rather than air travel. Most impressively, three Tasmanians cycled for three days from Hobart to Melbourne University (with the assistance of the Bass Strait ferry).

Education and networking were the focus of this three day gathering at Newman College within the University of Melbourne, where a plethora of distinguished speakers presented talks and interactive workshops to enlighten the receptive minds in attendance: academics, environmental activists, clinicians and all combinations of the three.

All present agreed that it was long overdue that medical students gathered to discuss environmental issues relevant to health; issues that for various reasons have been sidelined by the medical fraternity. These issues often traverse traditional subject boundaries, implying a perceived or real lack of academic expertise. Additionally, the lack of confidence in using one's 'authority' as a medical professional plays a part. Climate change, for instance, is often seen as a political or economic concern rather than a threat to health. Being too busy, self-preservation, fear over allegations of hypocrisy, ignorance, inertia and 'donor fatigue' all contribute to the reluctance of doctors to speak up.

Attendees with speakers Dr Forbes McGain (fourth from left) and Dr Peter Tait (fifth from left).

The result of one attendee's bright iDEA.

According to Costello *et al.*, climate change "is the biggest global health threat of the 21st century" and the repercussions to health will be global in reach, but with a disproportionately large impact falling on the developing world. [1] Matthew Wright, co-founder of Beyond Zero Emissions, a Melbourne-based organisation promoting the rapid transition to a zero carbon future, raised the interesting point that planning for a zero-carbon future is different to planning for a low emissions future, which, in turn, is different to planning for a doubtful emission reduction trading scheme in which concessions are made to big polluters. Although it seems paradoxical, government inaction in the short term could thus be preferable to legislating a hurried, binding scheme, that is in fact ineffectual in preventing an unsafe average global warming of two or more degrees.

Richard Di Natale, a former GP and Public Health physician, provided insight into how one might make the transition from clinician to environmental activist and politician. His non-linear career trajectory has seen him transition through positions in primary care, HIV programme development, Government Health Department bureaucracy and community-building. Most recently, he is persuading Victorian voters to give him the job of a Greens Senator at the next Federal election

In keeping with the activism theme, Sea Shepherd crew member and physician-in-training Dr Merryn Redenbach opened discussion on how one might oscillate between being a Paediatric Registrar at the Royal Children's Hospital (Melbourne) and ship doctor for the marine wildlife conservation organisation. In her case, one of these roles obliged her to spend time in a Canadian prison cell; a notice, perhaps, for those who are also in the process of placing deontological conviction above personal comfort.

However, action, political or otherwise, is not always the consequence of a firmly held conviction. Taegan Edwards, a Research Fellow from the University of Melbourne, explored the issue in relation to climate change. Emotional responses to absorbing dire information, such as fear of impending climate-induced doom, were discussed along with typical responses and coping mechanisms. Comments from the audience floor indicated that she had touched on a common experience; often relating to the truisms that change of any kind is not often simple and being green is not frequently convenient.

Enormous difficulty is not always insurmountable, and truth and justice do sometimes prevail against all odds as speaker Bill Williams demonstrated. The GP and President of the Medical Association for the Prevention of War (MAPW) reflected on his decade-long work as a campaigner for peace and nuclear disarmament. In the process, he managed to impart confidence in the delegates: things have and will continue to change for the better, particularly as long as those motivated by common good, rather than vested interests, find their voice and lead. His example provided a convincing case against leaving political engagement to professional lobbyists when it comes to issues that will truly shape our future.

Several speakers addressed the specifics of how the medical profession might choose to act on climate change. Colleen Hartland MLC, of the Victorian Greens, spoke about Melbourne's bushfire season and the prevalence and prevention of heat stress amongst the elderly. ANU academic Dr Colin Butler, co-founder and director of the Benevolent Organisation for Development, Health and Insight, discussed sustainability and global health, introducing the delegates to the primary, secondary and tertiary health effects of climate change and the complex interactions between them. Professor David Shearman, a physician and researcher from the University of Adelaide, led a roundtable forum on the potential for medical students to provide the necessary agitation for the medical establishment to embrace and normalise a new eco-health paradigm. Such a paradigm would place the natural world in its rightful place as not only a prerequisite resource for public physical health but as an end in itself of incalculable intrinsic worth. He conveyed that nature wears many hats - therapeutic and restorative, emotionally consoling, awe-inspiring, as well as providing a setting for physical exertion, food production, storage of drinking water and human settlement. Reflecting on how we can better interact within our ecosystem should be regarded as a central dilemma for the medical profession.

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Attendees engaged in roundtable discussion.

Those whose actions are already making waves in the medical sector include Monash medical student and AMSA Thinktank member Michael Loftus, and Dr Forbes McGain, a consultant anaesthetist at the Western Hospital in Victoria. Michael spoke about AMSA Thinktank's recent Climate Code Green campaign, resources for which included a highly-acclaimed short video (that was scheduled to be screened at COP15) and an accompanying booklet on health and climate change. Such achievements by fellow medical students emphasised to attendees that it is possible to make an impact from a grass-roots level. Dr McGain spoke about his seminal research into 'green hospitals', the excessive waste and unsustainable use of resources within our health system and the many ways our hospitals can improve their green credentials without compromising infection control and health care.

All in all, iDEA was a wonderful opportunity to hear from academics and doctors whose daily work enables them to explore the relationship between health and the environment. Many difficult questions were raised; no easy solutions were found. Despite this, the delegates left confident that in time solutions will be created and embraced. Moreover, many came to the realisation that the health sector has an important role to play in this process. As a starting point, doctors and medical students can address the unsustainable aspects of our profession and generate awareness and knowledge about what our responsibilities and potential contributions are, both as individuals and as professionals. Without this, we will not be able to achieve the changes that are needed.

The closing event of the conference was the election of the 2010 DEA student committee and planning for the year's events. With a wealth of inspiration to draw on, and a strong commitment to reducing the adverse impact of climate change on health, 2010 promises to be an exciting year.

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So you think you can research?

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Sina is simultaneously working towards an MD and working in the orthopaedics department at St. Vincent's Hospital, Melbourne.

I had always considered myself an exceptional dancer. In my mind, my dance moves were unparalleled. However, in reflection, I must admit that the majority of my moves were employed to impress the scrub-nurses by turning my gown in tune to the bopping background beat of the theatre iPod. However, my delusions of dancing grandeur were shattered after watching a number of the popular dance-based shows on television. I realised it took far more than genetic talent, which I still choose to believe I have in abundance, to make a dancer. It requires hours of practice combined with fitness, good music, choreography and originality to succeed. Research, it appears, is not too dissimilar.

I had never been the most proactive student and my CV was barer than a middle-aged German tourist holidaying in Thailand. I had reached a stage in my career where it was time to contribute to medical research. Those who partake in evidence-based medicine know how important research is to the field of medicine.

If you have ever considered undertaking some formal research yourself, here are a few lessons I learnt the hard way:

What do you need?

So, you want to research? Not sure where to begin?

In dance, you need to start with either good music or a good choreographer. In research, your music is your idea, question or inspiration, and your choreographer is your supervisor.

The music (idea)

The chances are that someone, somewhere, has already attempted to adapt "the sprinkler" to your chosen music. As in research, if you think you have a good idea, someone else may have had it before you. To find out, the next step is to conduct a literature review. Medline is a good place to start.

Don't be disheartened if someone has already researched your hypothesis. In medicine, most people can only answer very specific questions. So, if your good idea has already been partially covered, then read a few articles and find a more specific, unanswered question similar to your original one.

For example, if your question was "How effective is heparin in preventing DVT?" then refine your question to "How effective is low molecular weigh heparin in preventing DVT in male patients aged between 80 and 81 with a past history of smoking 22 cigarettes a day who have just undergone a knee replacement and whose favourite colour is light blue, when compared to Aspirin?" and believe you me, it is unlikely anyone else has researched that topic! Also, if someone has attempted to answer your question, it is worthwhile reading their article. If you find that their methodology is lacking, then you may decide to investigate that topic regardless, albeit with more watertight

P - patient, population

- What population would you like to research on?
- Do you have good access and sufficient numbers?
- A power-study may be helpful to determine how many participants you are likely to require.
- Beware underae children and pregnant women. Can be very difficult to get ethics.

I - Intervention

- What intervention are you seeking to research on?
- Is it new? Is it safe? Do you need ethics approaval?
- Do you have access to the intervention?
- Has it been tested before?
- How much will it cost?

C - Comparison

- What is the best available treatment currently?
- If none, can you use a placebo?
- Can you compare your intervention with this?

O - Outcome

- What outcomes best represent success?
- How can you test these outcomes?
- What statistical methods will you use to test these outcomes?
- Objectives vs. subjectives outcomes.
- Should be exact and comparable.
- Are your outcome measurements the same as the patient's?

***Figure 1**. Using the PICO system is a simple way of formulating a scientific question. [1]*

methods. Boosting the level of evidence is also looked upon favourably. If you find a case report, try and write a case series. If you stumble across a prospective study, aim for a randomized controlled trial.

Your music will need a tempo, a nice bass-line and of course catchy lyrics. Your idea/question will also need specific details. The best way to formulate a methodical question is to use the time-honoured PICO format. [1] PICO stands for Population, Intervention, Control, and Outcome.

The population should include patients you have easy access to. Also, it should include the subjects most likely to be present in your field of interest. For example, back to our DVT scenario, those requiring DVT prophylaxes are usually surgical patients, especially orthopaedic patients. Be wary of including minors or pregnant females in your population, as you will need to complete piles of paperwork to be given permission to use these subsets for research.

The intervention should be something you are interested in, and probably something that is slightly controversial, yet proven safe. Remember, most journals require evidence of Ethics Committee approval, and it is exceedingly difficult to gain approval for something seemingly dangerous or untested.

The comparison should be the current standard treatment. If no standard treatment exists, then the comparison should be with a placebo or control. But ultimately you should have a comparison or control. Research without this key component lacks validity. For example, instead of merely researching what percentage of DVT patients have the middle name Bob, you need to compare that to a control, that is, what percentage of the population with similar demographics has the middle name Bob.

The outcome should be clearly defined before the research begins. For example, are you looking at the number of DVT? The size of the DVT? The location of the DVT? The mortality and morbidity associated with DVT? The definitions and endpoints should be quite clear. Also, it is worth considering if your outcome measurements are the same as the patient's. For example, if a patient is feeling less pain with a certain drug but suffering many other new side effects, and your outcome is just pain-relief, then you may not be capturing the full picture. The patient may prefer a little more pain instead of all the new side effects!

The choreographer (supervisor)

Although the dancer does most of the legwork, the choreographer is the one behind the scenes who can make or break a routine. Likewise, a good supervisor is worth their weight in gold. A good supervisor should be knowledgeable, approachable and enthusiastic.

Choreographers usually specialise in a certain field of dance and are usually ex-dancers themselves. With knowledge of what works with what music, they know what is original and what has been done before and they have proven they are able to come up with a dance routine that the audience will like.

Your supervisor should be similar. They should be expert in your field of interest. They should know the best way to undertake the research. That is, how to design a study in a clinical trial, or how to go about laboratory work. They should be up-to-date with current knowledge and be able to help devise original ideas. Because of their past experience, their supervision should help validate your research and allow it to be noticed by the audience. Like the choreographer, the supervisor's role is to focus your raw talent and help you avoid common mistakes.

The best place to find a supervisor is to ask around. Find out who has been a supervisor in the past. They are usually associated with a major university and tend to be more academic. You could even ask your university if they have a list of previous supervisors. Or attend scientific meetings to spot potential supervisors. Then it is simply a matter of making a list and approaching each possible supervisor and discussing your research goals with them. You should have a basic idea of what you hope to achieve before you approach them. Then they can guide you in fine-tuning your idea and commenting on its feasibility. If they are too busy to hear your research proposal, then chances are they will be too busy to supervise you. A supervisor should be available when you need them, either to run a question by them, to review any articles you may have written and to give you feedback on what to do next.

Remember, you can always have more than one supervisor. The upside of this is that you can gain advice from different viewpoints, as each supervisor tends to concentrate on different aspects of the research. The downside is you have to appease both supervisors, and this can sometimes be difficult if they do not see eye-to-eye on certain matters.

Paying for your dance lessons (finance)

It's hard to become a professional dancer. While you are learning your steps, you need to have considered your financial position. Practice takes time and will likely consume the spare time usually reserved for part-time work. But you still need to put food on the table and dancing shoes on your feet.

Research is similar; it is always more time consuming than first envisaged. Generally, a little bit of financial backing makes research a lot easier. Depending on your research, the project itself can be either funded by a hospital department, from a government grant (http://www.arc.gov.au) or through private enterprise. Your supervisor would be the best person to speak to about your project funding, as they would have previous experience in such matters. There are also many scholarships available, through your university, your faculty, NHMRC (http://www.nhmrc.gov.au) or specialty groups such as the Cancer Council (http://www.cancer.org.au). Your university is the best place to start looking. You should investigate these options long before you are thinking of beginning a substantial research project, as the deadline for applying for these is generally many months in advance.

Working all day, dancing all night (time)

So, you would love to learn to dance, but never seem to have the time? It takes many hours of dedication to become a good dancer. Likewise, research is a huge time commitment. Even the smallest project can snowball to consume all your time. A rule of thumb in the research world is to always allow twice as much time as you think you will need. As a medical student, or junior doctor, it may already be hard to juggle a busy academic life and social life, let alone adding some research commitments. You may already feel like an overburdened horse! But remember, the more you progress in your career, the busier you are likely to become! So the earlier you start the better off you will be, not only as you will have more time, but because the research you complete will be invaluable in improving your resume and securing those sought after opportunities in the future. Looking back at my student days, only now do I realise how much spare time was available to me. A few hours a week (far less than you would spend watching television) can add up to a substantial project over a year.

If you are really time-poor you have two options: either choose a very simple project, such as a review article or case report, or take time off to commit to research. It can be very rewarding to take a year or two out of medicine to focus on research. This is compulsory at many universities in the form of a Bachelor of Medical Science or similar degree. Once out of university, a year off to complete a Masters degree by research can not only be enjoyable but also very rewarding for your career.

Ballet, ballroom, contemporary, hip-hop… I like them all (types of research)

So, you want to dance, but not sure what style suits you best? There are so many to choose from and all have their positives and negatives. Once again, research is similar.

Did you love chemistry during high school and enjoy playing around with chemicals? Then laboratory work may suit you. This type of research is commonly used to find better ways to treat cancer. Advantages include

flexible time commitment and mind-boggling scope. Disadvantages include the long hours spent with only a beaker for company.

Are you a physics nut who is in love with forces and motion? Then you may be more suited to biomechanical research. This is common way of researching prosthetics and sports medicine. Advantages include interacting with fun machinery and lots of modern tools. Disadvantages include costs associated with buying these tools and hence the limited number of biomechanical labs around.

Do you enjoy talking and working with patients and volunteers? Then you may also enjoy clinical research, where interaction with patients and colleagues is key to success. Advantages include patient interaction and discovery of instantaneously relevant clinical information. Disadvantages include total reliance on patients and colleagues following the projects instructions and difficulty in obtaining ethics approval.

Are you good with numbers and mathematics? Then epidemiological or population studies may be the best way to utilise your skills. Advantages include the ability to control your time, minimal overheads and ability to do small projects quickly. Disadvantages include the headaches associated with advanced statistics and large numbers.

No matter what pathway you choose, they are all rewarding in their own way. Yes, you will have your good days and you will have days you would rather forget, but in the end, nothing is as fulfilling as knowing you have contributed to your field. So take the challenge and like Isaac Newton, stand on the shoulders of giants and find out how far you can see!

Conclusion

Like dance, research can be extremely fulfilling. At first, it can be difficult to find your feet. But once the basic moves are learnt and confidence is gained, dancing becomes natural and you will find yourself the envy of your peers and colleagues in no time at all.

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