Volume 4, Issue 1 | 2013

Australian Medical Student Journal

The benefits of male HPV vaccination

A systematic review

Feature — Fiction and psychiatry - tale of a forgotten teacher

Case — Intracranial hypotension & postural headaches

Guest — Reaping the benefits of collaboration in medical research

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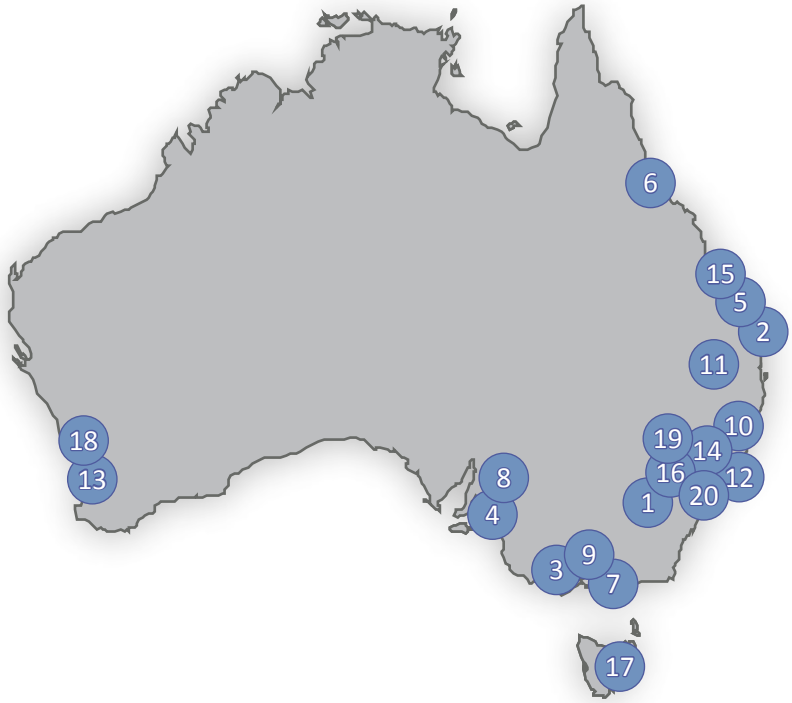

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Welcome from the AMSJ

Tahmina Anwari
Internal Director, AMSJ

Welcome to Volume 4, Issue 1 of the Australian Medical Students Journal (AMSJ).

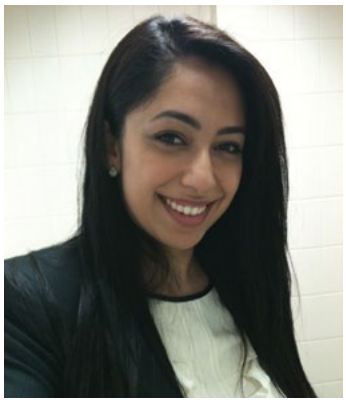
Yet again, we are pleased to offer our readers the opportunity to explore the opinions, reviews and research of their colleagues and to provide the avenue for our authors to publish their manuscripts. We are delighted to present to you our guest authors - Professor Leslie Bolitho, Professor Richard Larkins and Professor Michael Hollands – who have published manuscripts that are significant to the needs of medical students.

It is with great pleasure that I welcome our ever-growing new staff who have dedicated their time and effort in maintaining AMSJ as a prestigious journal. I extend a warm acknowledgement to all our staff, who have once again undertaken a remarkable job in bringing this issue together. As always we are grateful for all our sponsors who have allowed the medical students of Australia to experience the opportunity for academic growth and professional development.

A generous acknowledgement must be made to our out-going Executive Directors, Alexander Murphy and Grace Leo for their outstanding contributions to the AMSJ over the years.

It is with great pleasure that I undertake the role of Executive Internal Director for the AMSJ and I would like to welcome our incoming Executive External Director, Ha Lu.

We look forward to receiving submissions from all the Australian medical universities for our upcoming issues, and we hope you enjoy Volume 4, Issue 1.



Ha Lu
External Director, AMSJ

It is my pleasure to welcome you to Volume 4 Issue 1 of the Australian Medical Student Journal (AMSJ).

The AMSJ is the peak medical student publication in Australia. We have received submissions from all across Australia and again, the standard has been exceptional. It is also our honour to publish pieces from our guest authors Professor Richard Larkins, Professor Leslie Bolitho and Professor Michael Hollands.

The AMSJ is at the forefront of student research and continues to create unprecedented opportunities for students. The most important of course, is providing the platform for students to present peer-reviewed research to a national audience in our biannual journal. Looking into the future, the AMSJ will continue to rapidly expand opportunities for students. This will be done at a national level, through our National Executive, as well as at a state level by our University Representatives. I am excited and optimistic about the future of medical student research in Australia.

The AMSJ exists because of the enthusiasm of medical students from all around Australia. I encourage all students to engage with the AMSJ and contribute to it as a staff member, author and most importantly, as a reader.

I congratulate the entire staff for their stellar efforts in producing Volume 4 Issue 1. Particularly, I would like to acknowledge the work of Tahmina Anwari, the Internal Director, and Michael Thompson, the Editor-in-Chief.

Welcome to Volume 4 Issue 1. Sit back and enjoy this vast array of talent.

Ha Lu, Grace Leo, Tahmina Anwari and Alexander Murphy

The Australian Medical Student Journal: a nationwide endeavour

Michael Thompson
Editor-In-Chief, AMSJ

Welcome to Volume 4, Issue 1 of the *Australian Medical Student Journal.*

This issue of the *AMSJ* continues to develop our core aims of supporting medical student research by providing a dedicated journal for publication of outstanding medical student work and a focus on issues relevant to Australia in general and Australian medical students in particular. Key milestones for the *Australian Medical Student Journal* over the past months have included the online publication of the Australian Students' Surgical Conference, the expansion of our editorial team to include seven new members, each talented upcoming physician-scientists, and a broader expansion of our medical student staff. Senior *AMSJ* staff are now located in every state across Australian and there are representatives at each medical school.

This issue the *AMSJ* received an unprecedented number of outstanding submissions from medical students across the country. Some key highlights for this issue include a timely review by *Boulat* and *Hatwal* of the case for male HPV vaccination. This review, published as the Australian government announces its world first initiative of immunising young men against HPV, was identified by our editorial team and reviewers as a excellent review of an important contemporary public health issue and has been awarded the best article prize for Volume 4, Issue 1. Other notable submissions include a rigorous comparative review of anaesthetic methods for paediatric elective inguinal herniotomy, a synopsis of treatment options for preventing cardiac sequelae in Kawasaki disease, a reflective essay on the humanising influence of fiction in psychiatry, and a case report of spontaneous intracranial hypotension. Editorials by Saion Chatterjee and Janindu Goonawardena discuss structural changes occurring in academic publishing and the current challenges faced by the medical workforce across Australia. We are also privileged to host articles from prominent Australians: Professor Larkins, Chair of European Molecular Biology Laboratory-Australia (EMBL-Australia) and the Victorian Comprehensive Cancer Centre (VCCC), Professor Bolitho, President of the Royal Australia College of Physicians (RACP) and Professor Hollands, President of the Royal Australia College of Surgeons (RACS), to provide a top-down perspective on issues important to medical students.

Health and medical research in Australia faces key challenges including sustainability and international competitiveness. The recent McKeon Review of Health and Medical Research in Australia provides a framework for how Australian researchers can help to maximise the health of all Australians and contribute on a global scale. A major facet of this review is the emphasis on collaboration. In a country with a population less than one fiftieth of our neighbours, China and India, and public research expenditure less than one thirtieth of the United States, collaboration is an integral component to achieving global impact. In his guest article, Professor Larkins, Chair of EMBL-Australia and the VCCC, offers his advice and experience as the Chair of two leading collaborative research initiatives in Australia. With the upcoming federal budget and election, we also spotlight the issue of sustainability in the healthcare system. Professor Bolitho of the RACP provides a considered perspective on the measures required to accommodate increasing numbers of medical graduates. Professor Hollands of the RACS and Associate Editor Janindu Goonawardena provide complementary

perspectives on contemporary surgical training in Australia and discuss potential measures to address rural medical workforce shortages.

This issue of *AMSJ* represents the accumulation of many hours of voluntary work from *AMSJ* staff and reviewers. We have been privileged to lead a team of highly motivated, intelligent and hardworking medical students from across the country, without whom publication of this journal would not be possible. We would additionally like to thank our external peer reviewers, many who completed their first review this issue and many more who regularly contribute their time and expertise to the *AMSJ*. The initiative of publicly thanking reviewers will be continued this year, and their names published in the latter half of the year. Finally, we would like to thank all authors who contributed to the *AMSJ* and all our readers, who provide content and meaning to this publication. We hope you enjoy this issue and that it serves as motivation for medical students and nascent authors of future publications.

Thought the 'bed shortage' was bad, until the 'surgeon shortage' came along

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"Make up your mind how many doctors a community needs to keep it well. Do not register more or less than this number.''

George Bernard Shaw

If you have ever had the opportunity of finding yourself in a surgical theatre, the last thing you want to have on your mind are doubts about the person holding the scalpel. To ensure the highest professional standards are maintained, trainees of the Royal Australasian College of Surgeons (RACS) undergo a rigorous five to six year postgraduate training program prior to final qualification as a surgical consultant. [1] However, such a long and demanding training program has proven to be a double-edged sword for the surgical speciality. Studies have shown that one in four surgeons plan to retire in the next five years and that only sixteen percent of surgeons were under 40 years old. [2] The same study demonstrated that the average retirement age for surgeons has decreased by ten years. [2] These factors place an immense amount of pressure on surgical training programs, particularly in an era where the ageing population is creating more demand for surgical services. [2] While workforce shortage issues are by no means unique to the RACS, and indeed are felt by many medical colleges across Australia, this editorial will focus on the RACS to illustrate the issues affecting a broad range of medical specialities.

Along with many medical colleges around Australia, the RACS faces a looming workforce crisis with an ageing workforce approaching retirement and an ageing population with increasing healthcare needs, combining to create a critical demand for scarce services. The 2011 annual report published by the RACS highlighted that the number of first year surgical trainees across all specialties was 246 [3] compared to the 3000+ medical students graduating from around the country each year. While this represents a relatively small fraction of the available workforce pool, the RACS has taken the initiative to increase the number of surgical trainee positions by twelve percent compared to 2010. [3] Despite these gains, the RACS estimates that at least another 80 surgeons will have to graduate each year in addition to the 184 new surgeons currently graduating each year, in order to begin to redress surgeon workforce shortage. [4,5]

Low trainee numbers represent a composite of many factors, including financial limitations, need for skilled supervision and opportunity for practical experience. [6] The public sector has reached its full capacity for surgical training posts as such posts are funded by the State governments hence they are limited by budget provisions. [5] Consequently, underfunding, chronic shortage of nursing staff and lack of resources in public hospitals are seen as some of the main reasons for extended waiting times for surgery. [7] Due to the lack of such resources, it is a common trend now to see surgical lists being limited or procedures being cancelled because of time constraints. [7] Increasing the number of trainee posts will require significant fundamental changes, namely greater resourcing of the public health system. [6] To avoid the looming workforce crisis, governments will have to move quickly to ensure adequate training posts are in place across all medical specialties. [3,5] In Australia, more than 60% of elective surgery is in the private sector. [5] Novel training opportunities, such as those offered by the private sector, should also be considered as clinicians with the appropriate range and depth of experience required to train junior doctors are not limited to the public sector. [5] Lack of resources, funding, safe working hours and reduced clinical exposure are all elements that add to this crisis of looming workforce shortage. [6,8]

While there is a compelling argument to expand the number of trainee positions around Australia, the challenge is to maintain the highest standards for surgical trainees. [7] Emphasis on the number of training positions created is the priority of any college and is a crucial aspect in offering quality treatment in both the public and private hospitals. [7] However, increasing the number of trainees to accommodate and cope with surgeon shortage might result in reduced individual theatre time, which is not acceptable. [4,7] While this may relieve the workforce shortage, however, it would only create more specialists with limited exposure to a wide range of surgical presentations. [7] The aim of surgical training is to ensure that trainees progress through an integrated program that provides them with the highest professional responsibility under appropriate supervision. [9] This not only ensures exceptional quality but also enables trainees to acquire the competencies needed to perform independently as qualified surgeons. There are concerns nonetheless that if there is a

large intake of surgeon trainees it may favour 'quantity' of trained surgeons over 'quality'. [7] This is unacceptable, not only for the safety of our patients, but also in a world of increasing medico-legal implications and litigation. [7]

Another challenge affecting the surgical profession and surgical trainees is the issue of safe working hours. Currently, the reported working hours of the surgical workforce on average is 60 hours per week, excluding 25 hours per week on average spent on-call. [5] Although safe working hours are less of an issue in Australia than the rest of the world, it still affects surgical training. [10] Safety and wellbeing of surgical trainees is a top priority of the RACS. [7] Reduced trainee hours have been encouraged by research showing that doctor fatigue compromises patient care, as well as awareness that fatigue hampers learning. [10] Long hours traditionally worked by surgeons may result in concerns regarding safe working hours and the possibility that the next generation of surgeons will seek enhanced work-life balance. [4,7] Adding to the ominous shortage of surgeons, the challenge still remains whether surgical trainees can still assimilate the necessary clinical experience in this reduced timeframe. [7] More and more trainees place increased emphasis on work-life balance [5], making alternate specialisation pathways a real possibility that many consider.

Many, if not all, of the issues felt by the RACS across Australia are rarefied in rural Australia. Rural general surgery, much like its general practice counterpart, is facing an impending crisis of workforce numbers. [11] Despite increasing urbanisation, approximately 25% of Australians still live in rural Australia [12] and it is this portion of the population that is likely to be the first and worst affected

by any further constriction in medical workforce numbers. Single or two-man surgical practices provide service to many rural and remote centres. [11] However in many areas where surgical services could be supported, no trainee surgeon is available. [11] Many current rural surgeons are also fast approaching retirement age. [11] In past years retention of surgeons in rural communities has been strong. [13] The lifestyle benefits, challenges and rewards all combined, have ensured that a large amount of rural surgeons are growing old in the country. [13] However, this perception may well be a thing of the past. [13] Younger surgeons are more likely to consider time off on call, annual leave and privacy as lifestyle considerations which compel them back towards the metropolitan area. [13] Such a shift in attitude towards limiting one's workload combined with the continuing decline in Australian rural practices will apply various additional pressures on the rural surgeon workforce in the near future. [11]

Two main factors that determine if a trainee surgeon is more likely to pursue a rural career are the exposure to good quality rural terms as an undergraduate and having a rural background. [11,13] Selections for rural posts are more common in doctors from a country background who are more likely to return to, and remain in, a rural practice. [12,13] Acknowledging this factor, many Australian medical schools have now incorporated both mandatory and voluntary rural terms as a part of their curriculum. [11] In addition to these undergraduate initiatives, ongoing rural placements during postgraduate years may need to be established and given greater prominence. [11] A trainee being allocated to the same rural location over a period of years increases the possibility of the trainee settling in the same rural location following their training. [13] This may be due to familiarity with the social and cultural setting as well as the desire to provide continuous care for his/her patients. [13] As a result of these undergraduate and/or postgraduate initiatives, we can expect to witness the next generation of advanced surgical trainees with a foundation of rural experience, demonstrating a willingness to undertake rural terms as an accepted and expected component of their general surgery training. [11,13] These trainees may then choose to settle in the same rural location following training, thus decreasing the rural surgeon shortage.

The aim of surgical training is to ensure that trainees progress through an integrated program that provides them with increasing professional responsibility under appropriate supervision. [8] This enables them to acquire the competencies needed to perform independently as qualified surgeons. [9] The RACS has taken major steps to address its workforce shortage. Continuing efforts to provide for trainees and their needs are given place of prominence in the RACS 2011-2015 strategic plan. The RACS' role in monitoring, coordinating, planning and provisioning of services, as well as obtaining adequate funding for surgical training programs, remains a major responsibility of the College. Emphasis on rural rotations at an undergraduate and early postgraduate level, consideration of the work-life balance of both trainees and surgeons and sufficient staffing of theatres, will help eradicate the surgeon shortage whilst ensuring that the finest surgical education and care is available to Australians into the future.

Conflict of interest

None declared.

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Freedom of information

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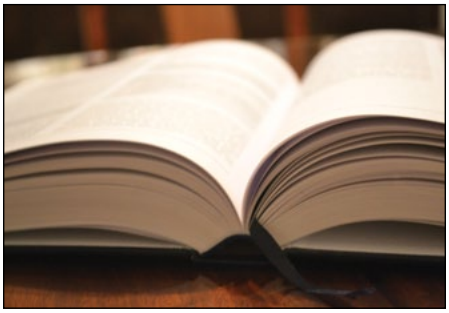
Early last year, a David and Goliath battle raged between the most unlikely of foes. The gripes of a single blog post inspired a group of disaffected mathematicians and scientists to join forces and boycott the world's largest publisher of scientific journals, Elsevier. Their movement, dubbed "Academic Spring", was in response to the company's political backing of the Research Works Act, a proposed bill in the United States (US) aimed at denying public-access to scientific research funded by the US National Institute of Health (NIH). Drafted solely to benefit the interests of publishing companies, Elsevier reneged on its support for the bill following months of escalating protests and scathing publicity. Though the bill never saw the light of day, the struggle that unfolded was symptomatic of a more deep-seated and pervasive conflict between academics and publishers; a conflict that has been thrown into sharp relief by the rise of online publishing.

Since the publication of the first scholarly journal in 1665, journals have played an integral role in the scientific process. [1] As vanguards of modern day science, journals have been an enduring and authoritative source of the latest scientific research and developments. Academics form a key ingredient in the turnover and success of journals. Not only are they responsible for generating content, but they also volunteer as peer-reviewers for submissions relevant to their field of expertise and as mediators of the editorial process; a peculiar arrangement that plays into the hands of publishers. Before the arrival of the internet, journals facilitated the quick and widespread exchange of information throughout the scientific world. Publishers performed services including proofing, formatting, copyediting, printing, and worldwide distribution. [1] The digital age, however, rendered many of these tasks redundant and allowed publishers to dramatically reduce their costs. [1] Publishers also used the opportunity to offload further responsibilities onto the shoulders of academics, such as formatting and most copyediting, in order to significantly increase profits despite playing a limited role in the journal's overall production.

The changing landscape of scientific publishing has seen commercial publishing firms acquire a lion's share of the market from not-for-profit scientific societies in the last few decades. [2] The resulting monopolistic stranglehold has led to exorbitant subscription fees for access to their treasury of knowledge. Profit margins have hovered between 30-40 percent for over a decade, due in part to subscription prices outpacing inflation by seven percent per annum. [3] Moreover, publishers have exploited the practice of offering journals subscriptions in bundles, rather than on an individual needs basis, a crucial ploy underlying their profits. [4] Long-standing price increases, accompanied by dwindling library budgets, have gravely hampered the ability of libraries, universities, and investigators to acquire the most up-to-date publications necessary for research and education. [4] The total expenditure on serials by Australian university libraries in 2010 was a staggering AU$180 million. [5] Even the most affluent libraries, such as Harvard, are declaring the situation as untenable and are resorting to subscriptions cuts. [3]

Along with cost, the principle of access for clinicians, scientists, and the general public alike underscores the ensuing debate. There is little argument that the accessibility of scientific findings is critical to the advancement of scientific progress. Consequently, the great paywalls of publishing houses have fostered an environment that stagnates the translation of science to the bedside and stifles medical innovation. Peer-reviewed literature is often funded by taxpayer-supported government grants. In Australia and New Zealand, over 80% of research and development is funded by the public purse. [6] In effect, governments have been held ransom by firms privatising the profits accruing to publicly-financed knowledge. The barriers of access and cost also extend to developing nations. Without access to reliable medical literature, efforts to develop sustainable health care systems in these regions are severely undermined.

Researchers are equally culpable for their current plight. Typically, works of intellectual property warrant financial remuneration. However, writing for impact instead of payment has become both intrinsic and unique to academic journals, a paradigm from centuries before when journals were unable to pay authors for their work. [3] Impact, a proxy measure developed by commercial publishers, reflects an academic journal's visibility for a given year. It is derived from the ratio between the average number of citations per article received during the two preceding years and the total number



of articles it published during the same period. [7] The higher the impact factor of a journal, the greater its clout and influence. The importance placed on impact factor has become ingrained in the collective psyche of academia. Academics are competitively assessed on their publication record in scientific journals to secure grants and advance their careers. Inevitably, researchers have become servile to an archaic system, which serves only the interests of commercial publishers.

Open access (OA) represents a new business model in the academic journal industry, underpinned by the growth and reach of the internet. It provides unfettered online access to all research material, as well as the right to copy and redistribute it without restrictions. [1] Open access (OA) uses two channels of distribution: the "gold" or the "green" paths. [1] The "gold" path publishes articles in freely available OA journals that maintain peer review to preserve their academic reputations. The Public Library of Science (PLoS) and BioMed Central (BMC) are leading examples of OA publishers. The "green" path requires authors to self-archive their work on an online repository, available free of charge to the public. [1] Table 1 highlights some of the differences between traditional and OA journals.

Open access (OA) offers many advantages compared to traditional journal publishing. Evidence shows that OA has substantially increased the amount of scholarly work available to all, regardless of economic status or institutional affiliation, increasing the probability of research being read and, accordingly, of being cited. [8] Open access (OA) can integrate new technological approaches such as text mining, collaborative filtering, and semantic indexing, and has the potential to encourage new research methodologies. [8] A significant bone of contention with traditional journals has been

Table 1. *Comparison of traditional and OA journals. [11]*

	Traditional journals	Open access (OA) journals
Peer-reviewed	Yes	Yes
Pay-to-publish	Some	Yes
Subscription fees	Yes	No
Degree of access	Controlled; content available only to subscribers or through consortia (e.g., OVID)	All content available to anyone with internet access
Speed of review process	Time varies from submission to first decision	Typically rapid; usually under 21 days to first decision
Speed of publication	Depends on production schedule	Typically rapid; within weeks of acceptance, sometimes less; articles do not have to be prepared for print publication

the need for authors to relinquish copyright of their material. Open access (OA) allows authors to retain copyright, and provides readers and other authors with the rights to re-use, re-publish, and, in some cases, create derivatives of their work. [8] Furthermore, OA bridges both the digital and physical divide between the developing and developed worlds, mitigating some of the limitations faced by scientists in low-income countries to publish their work. Institutional repositories and OA publication fee waivers have been instrumental in promoting their research profile onto the international stage, by shedding the burden of cost. [9]

Despite offering free access to readers, OA has been plagued by its share of criticism. Traditional publishing firms, one of its fiercest opponents, contend that OA journals shift the cost of production from consumer to author, with fees ranging from $1,000-5,000 per article. [3] Whilst levelling this critique, commercial firms overlook the fact that they also foist publication fees onto authors which may even exceed the costs of OA journals. [1,3] Publication costs are now a common element in grant fund applications, and authors incur minimal to no charge. Inevitably, ethical concerns also arise from the OA model. The author-pay model may compromise the peer-review process as journals become financially dependent on researchers to publish articles. However, these concerns have been assuaged in recent years, due to the widespread number of high-quality OA journals that employ robust peer-review on par with their subscription counterparts. [1] The "green" route also poses problems for authors who may not possess the technical capabilities or resources to self-archive articles.

Open access (OA) represents the fastest growing business model for academic journals, and is likely to remain sustainable in the long-term. Many OA journals are now highly trusted, referenced, indexed, and well received. Its support has been bolstered by the evolving mandates of research funding agencies, including Australia's National Health and Medical Research Council (NHMRC), the United Kingdom's Wellcome Trust, and the NIH, placing research funded by their grants into the public domain within a year of initial publication. [7,10] Major data aggregators are also facilitating this trend, including PubMed and OVID, releasing OA databases and platforms dedicated to OA material. [11] Estimates project that 60 percent of all journal content will be published in OA journals by 2019. [11] Moreover, OA journals are rapidly approaching the same scientific impact and quality as subscription journals, particularly in the field of biomedicine, as suggested by one study. [7] Many have opined that OA could redefine measures of impact, using additional metrics such as number of downloads, bookmarks, tweets, and Facebook likes. Proponents of OA have turned their attention to how corporations like drug and chemical companies can support its efforts, which benefit from free access while contributing only a small subset of scientific articles and fees overall.

The advent of the internet has created a realm of possibilities for some and a minefield of challenges for others. Journals have navigated such obstacles for centuries, embracing new opportunities and adapting to change. Although the internet has effectively transformed publishers into "de facto" gatekeepers of their lucrative commodity, it has also been the impetus behind the OA revolution, proving to be a more cost-effective and equitable alternative to traditional publishing. But while OA continues to develop into the mainstay of journal publishing, perhaps its most immediate impact will be to diversify competition and precipitate a cultural change within the industry that sees science re-emerge at the forefront of its interests.

Conflict of interest

None declared.

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Pentraxin 3 – A new player in twinning frequency

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Grace has had a passion for research since high school, when she was given the opportunity to work with a research team at a major Brisbane hospital. She has a particular research interest in the gene interplay involved in adipocyte differentiation and its implications on obesity.
Grace hopes to fulfil the bench-to-bedside philosophy during her career, where she can use her passion for scientific research to improve patient treatment.

The conception of dizygotic twins is a complex trait.

It is thought to be influenced by a variety of environmental and genetic factors and displays significant regional variation in prevalence worldwide. [1] For example, in Sub-Saharan areas of Africa, twinning is very common (~23 per 1000 pregnancies), while in Asia twinning is much rarer (~5-6 per 1000 pregnancies). [2] Recent research has sought to determine the reasons behind the increased frequency of twinning in regions of Sub-Saharan Africa. Independent studies of women from Gambia and Upper East Ghana have given insight into gene mutations which may possibly increase the fertility of women and hence the frequency of twinning. Specifically, it was found that certain single-nucleotide polymorphisms (SNPs) in the gene of pentraxin 3 (PTX3), a key player in human fertility and innate immunity, occurred in higher frequency amongst the mothers of twins. [3] This report will review the known functions of PTX3 in immunity and fertility and their relation to twinning frequency.

Pentraxin 3 in innate immunity

PTX3 is a soluble pattern recognition receptor, which belongs to the acute phase reactants superfamily. [4] In the innate immune response, PTX3 is produced in response to primary pro-inflammatory signals such as interleukin 6 (IL-6) release or toll-like receptor activation. [5] It participates in immunity by recognising pathogens, facilitating complement activation and opsonisation. [6] Indeed, it is involved in immune defence against *Aspergillus, Pseudomonas, Salmonella, Mycobacterium tuberculosis*, cytomegalovirus and influenza. [7-9] Known mechanisms of anti-pathogenic action include the binding of sialylated ligands on PTX3 to membrane proteins such as haemagglutinins found in influenza viruses and cytomegaloviruses. As haemagglutinins are used by viruses for fusion and entry to host cells, the binding of PTX3 ligands to the haemagglutinins can block this function and hence lower the chance of viral infection. [7,8] The anti-viral actions of PTX3 against cytomegalovirus can also activate downstream immune components such as interferon regulatory factor 3 (IRF3) and the interleukin-12/interferon gamma (IL-12/IFN)-γ-dependent effector pathway, which in turn heighten anti-fungal defences against species such as *Aspergillus*. [8] Previous experiments performed by Garlanda et al. also show that PTX3-null mouse models were more susceptible to fungal infections, suggesting that PTX3 plays a non-redundant antifungal role. [10]

Pentraxin 3 in fertility

PTX3 is not only a major player in immunity, it has also been demonstrated to be linked to fertility in various studies. Specifically, PTX3 interacts with proteins such as TNF-stimulated gene 6 (TSG6) and inter-alpha-trypsin inhibitor (IαI) to form multimolecular constructs which facilitate cross-linking in the hyaluronan matrix that surrounds the cells of the cumulus oophorus. [11] This is crucial to the stability and organisation of the cumulus matrix, as shown in animal studies where PTX3-null mice produced ova with abnormal cumulus oophorus, which led to lower litter counts. [12,13] The infertility resulting from PTX3 knockout is not surprising as a functional cumulus oophorus is required for oocyte maturation, movement to oviduct and penetration by sperm. [14-16] Notably, mouse and human PTX3 are highly conserved, suggesting that PTX3 may play a similar role in humans. [4] Further supporting the key, non-redundant roles of PTX3 in fertility is the finding that PTX3 is one of the most highly upregulated genes during the pro-inflammatory cascade at the foetal-maternal interface, which is crucial to decidualisation, blastocyst invasion, anchorage and implantation. [17-20]

Pentraxin 3 in twinning

It is clear that PTX3 plays a crucial role in immunity and fertility. Tying all these findings together is research by Sirugo et al. and May et al. which demonstrate associations between twinning, female fertility and PTX3 SNPs in humans. [3,21] Sirugo et al. demonstrated that the frequency of certain PTX3 haplotypes differed in frequency between mothers of twins and mothers without twins in a sample of 130 Gambian sister pairs ($p = 0.006–3.03x10^{-6}$, depending on haplotype). [3] In concordance with this, data from May et al. based on a population study suggest that those findings may indeed be due to increased fertility conferred by the PTX3 mutations. [21] It was found that women with more than12 children had SNPs in PTX3 causing the highest production of PTX3 and that women with less than 2 children had SNPs which conferred the lowest production of PTX3. Specifically, rs6788044 SNP, which was associated with the highest PTX3 production ($p = 0.003$), was also associated with the highest fertility ($p = 0.043$). In addition, increased *ex vivo* LPS-induced PTX3 production, suggesting better immunity, was also associated with increased fertility ($p = 0.040$). [21]

Could complex gene interplay be the reason for higher rates of twinning in Sub-Saharan Africa?

Conclusion

Taken together, the data suggests that PTX3 may contribute to the high rates of twinning in Sub-Saharan Africa. As increased PTX3 expression confers improved innate immune response, local selective pressures due to disease may skew epigenetic controls to favour these particular variants in particular populations where a strong immune response is crucial. [3] Certain SNPs of PTX3 which are selected for also confer increased fertility, via mechanisms such as increased cumulus oophorus stability and regulation of the pro-inflammatory cascade of implantation. While the role of PTX3 in multiple ovulations - a primary factor of dizygotic twinning - is still unclear, the contribution of PTX3 to successful implantation is also vital to twinning, by increasing the chance of survival of multiple blastocysts. In conclusion, the available evidence suggests that PTX3 may be an important contributor to twinning, at least in some African populations.

Conflict of interest

None declared.

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Management of high-grade vulvar intraepithelial neoplasia

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Sylvia graduated from the University of New South Wales in 2012 and is currently working as an Intern at St George Hospital. She wrote this article during her final year of medical school and hopes to pursue Physician Training.

Vulval intraepithelial neoplasia (VIN) is a condition which is increasingly prevalent, particularly in young women, [1] but is a topic rarely touched upon in medical school. The following article reviews current treatment methods for VIN, both surgical and pharmacological, as well as promising new treatment modalities still being researched.

VIN is a condition in which pre-cancerous changes occur in the vulval skin. The incidence of the diagnosis of VIN is approximately 3/100,000, increasing more than four fold since 1973. [2] Vulvar intraepithelial neoplasia is classified into two main groups based on morphologic and histologic features, consisting of VIN usual group and VIN differentiated type. VIN usual group can be subdivided into basaloid and warty subtypes, typically occurs in younger, premenopausal women and is related to HPV infection and cigarette smoking. VIN differentiated type typically occurs in postmenopausal women and is often associated with lichen sclerosus, which presents as white patches on vulval skin. The rate of progression to invasive vulvar cancer in women with untreated high-grade VIN is reported to range from 9.0 to 18.5%. [3] Half of women with VIN are symptomatic, with pruritis, perineal pain or burning, dysuria, a visible lesion or a palpable abnormality. The lesions themselves are often multifocal, raised and can vary in colour from white to red, gray or brown. Diagnosis involves a colposcopic examination, where VIN lesions produce dense acetowhite lesions with or without punctuation. The goals of treatment are prevention of progression to invasive vulvar cancer and symptom relief, as well as preservation of normal vulvar function and anatomy.

Current surgical therapies include excisional treatments or vulvectomy. The main advantage of excisional therapies over ablative or medical treatment is the ability to make a histopathological diagnosis based on the excised lesion, particularly as occult invasive squamous cell carcinoma is present in many of these women. [4]

Wide local excision is the preferred initial intervention for women in whom clinical or pathologic findings suggest invasive cancer, despite a biopsy diagnosis of VIN, to obtain a specimen for pathologic analysis. [4] Localised high-grade VIN lesions are best managed by superficial local excision of an individual lesion, with reported recurrence rates of 20 to 40%. [5]

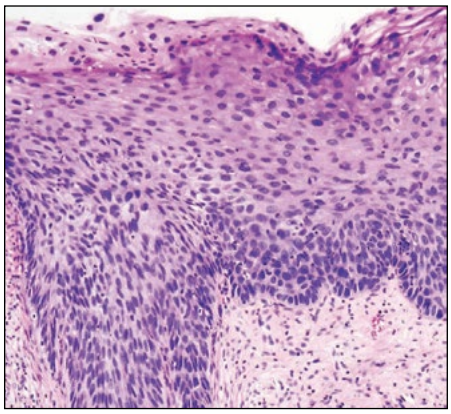
Multifocal or extensive lesions that are not amenable to removal with local excision are best removed with a partial or simple vulvectomy. This involves removal of part of or the entire vulva, respectively, together with subcutaneous tissue and perineal tissues if indicated; [5] a last resort as neither normal function nor anatomy are preserved.

Laser ablation therapy is an alternative to excisional therapy, particularly for women with multifocal and extensive disease in whom cancer is not suspected. [6] CO_2 laser vaporisation has been shown to be effective in eradicating VIN while achieving good cosmetic and functional results, with success rates of 40 to 75%. [6-7]

A systematic review showed that there were no significant differences in recurrence after vulvectomy, partial vulvectomy, local excision or laser evaporisation. [8]

Medical therapies aimed at preserving the vulvar anatomy are useful in younger patients, provided colposcopic examination and biopsies have excluded invasive disease. The primary medical treatment available is Imiquimod 5% cream, which has antiviral and antitumour effects via stimulation of local cytokine production and cell-mediated immunity. [9] A Cochrane review [1] concluded for women with high grade VIN, Imiquimod was better than placebo in terms of reduction in lesion size and histologic regression. This conclusion was based on the findings of three randomised placebo-controlled trials, with the largest trial reporting a complete response rate of 35% and partial response of 46%. [10] Common side effects reported were erythema, soreness, itching, burning, ulceration and flu-like symptoms; however, these side effects were be reduced by placing patients on an escalating dosing regimen. [1]

Agents such as cidofovir, 5-fluorouracil and photodynamic therapy are currently being investigated as treatment for vulval



intraepithelial neoplasia. Cidofovir is an acyclic nucleoside analogue with antiviral activity, and a pilot study shows promising results. [11] 5-fluorouracil is a chemotherapeutic agent that inhibits DNA synthesis, with a review demonstrating a remission rate of 34%; [12] however, this agent is used less commonly in current practice. Photodynamic therapy, whereby a sensitizing agent is applied prior to irradiation of the vulva, has been demonstrated to cause complete response in 33 to 55% of patients with VIN 2-3. [7,13]

The major surgical interventions for VIN appear to be similarly effective and are appropriate when there is desire for a histopathological specimen to exclude invasive cancer. Medical interventions are useful when occult cancer is unlikely and preservation of normal vulvar anatomy is desired. Evidence appears to be strongest for Imiquimod as a conservative medical intervention for the treatment of high grade VIN. Other promising agents include cidofovir, but further investigation through large scale studies is required to characterise the efficacy of these therapies. Diligent follow-up is essential in detecting disease recurrence and monitoring the effectiveness of therapies. More research is needed to develop effective treatment strategies that preserve function and anatomy, particularly as the disease becomes more prevalent in young women.

Conflict of interest

None declared.

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Adult pertussis vaccinations as a preventative method for infant morbidity and mortality

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Talia is a country-born and bred medical student who is passionate about general practice, specifically rural and remote medicine. She hopes to follow this interest by becoming a rural generalist with specialist skills in areas such as obstetrics and gynaecology.

Pertussis, or whooping cough, is a potentially fatal respiratory illness caused by the *Bordetella pertussis* bacteria. It commonly occurs in infants who have not completed their primary vaccination schedule. [1]

Since 2001, Australia's coverage rate with the three primary doses of the diphtheria, tetanus and acellular pertussis-containing vaccine (DTPa) at twelve months has been greater than 90%. [2] Despite this high coverage rate, there has been a sharp increase in the incidence of pertussis. In 2008, the Victorian Government received notification of a 56% increase in reported cases (1,644 cases in 2008 compared to 1054 cases in 2007). That same year, New South Wales also reported over 7,500 cases, more than tripling their 2007 total. [3] Given these startling statistics, we must ask ourselves why we are seeing such a significant rise in the incidence of pertussis.

One well researched explanation for this increase is that the pertussis vaccine is not conferring lifelong immunity. A North American study investigating the effectiveness of the pertussis vaccine found that there was a significant increase in laboratory-confirmed cases of clinical pertussis in children aged eight to 13 years. This correlated to the interval after the end of the preschool vaccinations. [4] Other studies have suggested that immunity can wane anywhere between three to 12 years post vaccination, creating ambiguity as to when we become susceptible again. [5,6] This limitation is due to the current non-existence of a clear serologic marker correlating with protection from pertussis. Approximately two years after vaccination, pertussis toxin antibodies have reached minimal levels; however, protection from the disease remains. This suggests immunity is multifactorial. [5]

Despite this, there is widespread agreement that adults with waning immunity and who are in close contact with non-immune infants are a major source of transmission. [6,7] In 2001, a study was published which analysed the source of infection in 140 infants under the age of twelve months who had been hospitalised for pertussis. In the 72 cases where the source of infection could be identified, parents were the source in 53% of cases and siblings accounted for another 22%. [8] The Australian paediatric surveillance unit study of 110 hospitalised infants with pertussis demonstrated adults to be the source in 68% of cases, 60% of which were the parents of the infant in question. [9] Other potential sources that have been identified include grandparents and paediatric health workers. [6]

Since the establishment in 2001 of the international collaboration, the Global Pertussis Initiative (GPI), strategies to decrease the incidence of pertussis have been extensively discussed, with particular emphasis on reducing adult transmission to unprotected infants. [6] In general it has been noted that the control of pertussis requires an increase in immunity in all age groups, especially in adults. [10] Although the GPI agrees that universal adult vaccination would be an effective strategy to protect non-immune infants, this would be too difficult to implement. [2,8] Furthermore, we must be aware that the success of herd immunity is dependent upon the level of population coverage and also the degree of contact between the infected and the non-immune infants. [11]

Due to the difficulties with implementing universal adult vaccinations, more targeted vaccination strategies have been proposed. [10] The concept of a 'cocoon' strategy, in which adults in close contact with unprotected infants are given booster vaccinations, [11] has been trialed throughout Australia in various forms. [12] This strategy is simpler to implement, as new parents and family members are easier to access via their contact with health services and their motivation to protect their children. [6] Moreover, because of this motivation, it may be reasonable to assume new parents would be willing to pay for this vaccine out of their own pockets, reducing the economic burden of the increased use of vaccines on our health system.

One model has suggested routine adult vaccination every ten years from the age of 20 years, combined with the 'cocoon' strategy of vaccination, would best reduce the rate of infant pertussis infections. However, to date there are no clinical data confirming this strategy to be effective. [11] Furthermore, this particular model is unlikely to receive public funding due to the large expense required.

Another strategy, recently recommended by the Advisory Committee on Immunisation Practices (ACIP), is that of implementing maternal vaccinations. The ACIP reviewed data in 2011 that showed preliminary evidence that there were no adverse effects after the administration of the pertussis vaccine to pregnant women. This strategy would significantly reduce the risk of infection to infants before they were even born. [13]

As one can see, the question of how to increase immunity in our community is complex, given that current strategies are expensive and difficult to implement. As infant deaths from pertussis are easily avoidable, developing effective preventive strategies should be of high priority.

Conflict of interest

None declared.

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A modern, effective and user-friendly approach to medical learning: an overview of spaced repetition programs

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Anton is interested in medical education, sports medicine and orthopaedics. He is passionate about helping others to discover ways of improving their learning skills. He also enjoys long walks along the beach, ice-creams in summer, and hopes one day to live out a day in the life of a slug, by bathing himself in cooking oil and sliming about.

Effective and efficient methods of learning are important for medical students to tackle the plethora of information available. A technique that is gaining increasing popularity is Spaced Repetition Learning.

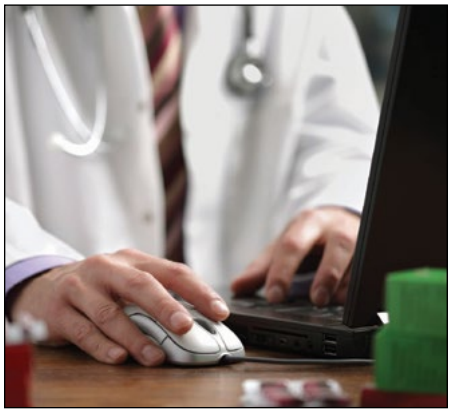
Spaced Repetition Learning (SRL) enhances retention by addressing our poor ability to process and retain information presented en mass at a single point in time. [1] Information is presented at varying time intervals depending on the student's evaluation of their ability to recall facts. [2] The benefits of this technique have been shown in numerous studies. In mild Alzheimer's disease, SRL proved useful for improving retention, visual memory and source recognition. [3,4] Another study compared massed versus spaced delivery of information to gastroenterology residents, who on assessment with multiple-choice quizzes showed enhanced long-term retention of facts with SRL. [5] Kerfoot et al also conducted several studies that demonstrated the applicability, efficacy and long-term durability of SRL teaching for urological trainees. [6-8]

Unfortunately, there is relative paucity of randomized trials involving medical students. A handful of studies conducted by Kerfoot et al have shown SRL significantly increases the effectiveness of learning. [9-11] One notable study in particular found that medical students using SRL were able to achieve the same results with significantly reduced study time, thus increasing the efficiency of study. [10] On the contrary, a well-constructed study has disputed the long-term effects of SRL, presenting evidence that the effects are primarily short-term. [12]

Several computer programs readily available use SRL methods, two of which are Anki and Mnemosyne. [13-15] Both programs are free to use (exception: Anki on iOS) and both allow an import and export of data in addition to supporting unicode, images, audio and LaTeX format. Anki also has the capacity to synchronise between devices, support video format and have multiple sides per card (Mnemosyne has a maximum of 3 sides per card). Both programs have cross-platform availability, and data from Mnemosyne is used to aid long-term memory research. [15]

To expand upon the use of Anki, with which the author has had more experience: it is a flashcard program that displays cards at varying intervals depending on how well one feels they have answered them in the past. Comprehensive and easy to understand instructions are available through the website, but in summary, the user writes a question and answer, and saves it to a 'deck' of cards. Each question can be labeled with one or more keywords (eg: 'cardiology'). Cards with a certain label can be reviewed exclusively or excluded from reviews as desired. Decks of cards can also be shared to Anki's online database or with other individuals. To begin learning without creating a new deck, downloading the "UK Finals Medicine" deck is a good starting point. There is also a varied range of other topics available including foreign languages, geography and musical instrument practice.

When reviewing a deck, the user is presented with a question (Figure 1), answers it (out loud, on paper, in their head) and clicks the mouse to view the answer. The user then grades their performance (Figure 2) and this is when spaced repetition theory is employed. By clicking "Again," the card will automatically become due at the end of that review session. Clicking "Easy" the first time a particular card is answered will make it due in about a week. Each successive time a card is answered correctly, the card's due date is pushed further into the future. Useful question examples for



a complaint, such as chest pain, may include differential diagnoses, history questions, physical examination and investigations. For a disease, such as COPD, question prompts may include: definition, epidemiology, pathophysiology, aetiology, symptoms, signs, investigations, management, prognosis/staging and complications.

After using Anki for over a year, several benefits have become apparent. It ensures consistent new learning whilst refreshing the student of prior knowledge. Setting review deadlines and adhering to them means one can learn many facts effectively, which saves precious time. Answering questions out loud is perhaps the most effective way to clarify thoughts and consolidate your understanding of a topic. It is also particularly helpful for OSCE examination preparation. Another benefit is the accessibility of Anki, as it is available on most smart phones and can synchronise between devices and computers. The main shortfall of using SRL programs is that its efficacy depends on user commitment.

In summary, Spaced Repetition Learning has been shown to be an effective learning tool in research studies. There are a number of software programs currently available that

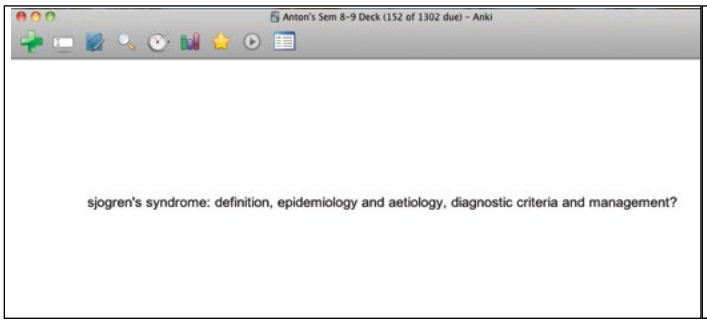


Figure 1. *Screen capture of Anki showing an example question before the answer is seen.*

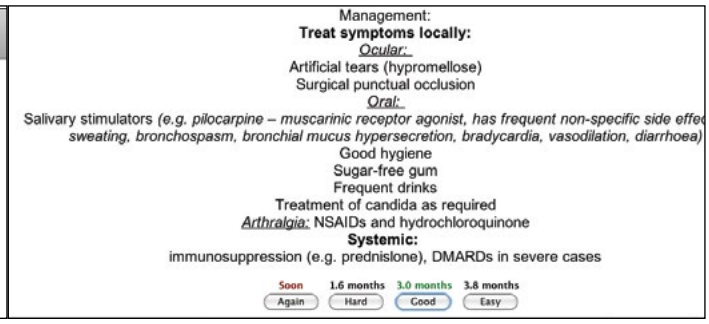


Figure 2. *Screen capture of part of the answer to Figure1 and options for self-assessment.*

are user friendly and free to use. From the author's personal experience and literature review, the success of SRL should certainly be applicable to medical students and I look forward to seeing further objective research in the future to support its use.

Conflict of interest

None declared.

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Paediatric regional anaesthesia: comparing caudal anaesthesia and ilioinguinal block for paediatric inguinal herniotomy

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Caudal anaesthesia and ilioinguinal block are effective, safe anaesthetic techniques for paediatric inguinal herniotomy. This review article aims to educate medical students about these techniques by examining their safety and efficacy in paediatric surgery, as well as discussing the relevant anatomy and pharmacology. The roles of general anaesthesia in combination with regional anaesthesia, and that of awake regional anaesthesia, are discussed, as is the administration of caudal adjuvants and concomitant intravenous opioid analgesia.

Introduction

Inguinal hernia is a common paediatric condition, occurring in approximately 2% of infant males, of slightly reduced incidence in females, [1] and as high as 9-11% in premature infants. [2] Inguinal herniotomy, the reparative operation, is most commonly performed under general anaesthesia with regional anaesthesia; however, some experts in caudal anaesthesia perform the procedure with awake regional anaesthesia. Regional anaesthesia can be provided via the epidural (usually caudal) or spinal routes, or by blocking peripheral nerves with local anaesthetic agents. The relevant techniques and anatomy will be discussed, as will side effects and safety considerations, and the pharmacology of the most commonly used local anaesthetics. The role of general anaesthesia, awake regional anaesthesia and the use of adjuvants in regional anaesthesia will be discussed, with particular focus on future developments in these fields.

Anatomy and technique

The surgical field for inguinal herniotomy is supplied by the ilioinguinal and iliohypogastric nerves, arising from the first lumbar spinal root, as well as by the lower intercostal nerves, arising from T11 and T12. [3] Caudal anaesthesia is provided by placing local anaesthetic agents into the epidural space, via the caudal route. It then diffuses across the dura to anaesthetise the ventral rami, which supply sensory (and motor) nerves. Thus, the level of anaesthesia needs to reach the lower thoracic region to be effective. The caudal block is usually commenced after the induction of general anaesthesia. With the patient lying in the left lateral position, the thumb and middle finger of the anaesthetist's left hand are placed on the two posterior superior iliac spines, the index finger then palpates the spinous process of the S4 vertebra. [4] Using sterile technique, a needle is inserted through the sacral hiatus to pierce the sacrococcygeal ligament, which is continuous with the ligamentum flavum (Figure 1). Correct placement of the needle can be confirmed by the "feel" of the needle passing through the ligament, the ease of injection and, if used, the ease of passing a catheter through the needle. The absence of spontaneous reflux, or aspiration, of cerebrospinal fluid or blood should be confirmed before drugs are injected into the sacral canal, which is continuous with the lumbar epidural space. [5]

Ilioinguinal block is achieved by using sterile technique to insert a needle inferomedially to the anterior superior iliac spine and injecting local anaesthetic between the external oblique and internal oblique muscles, and between the internal oblique and the transversus

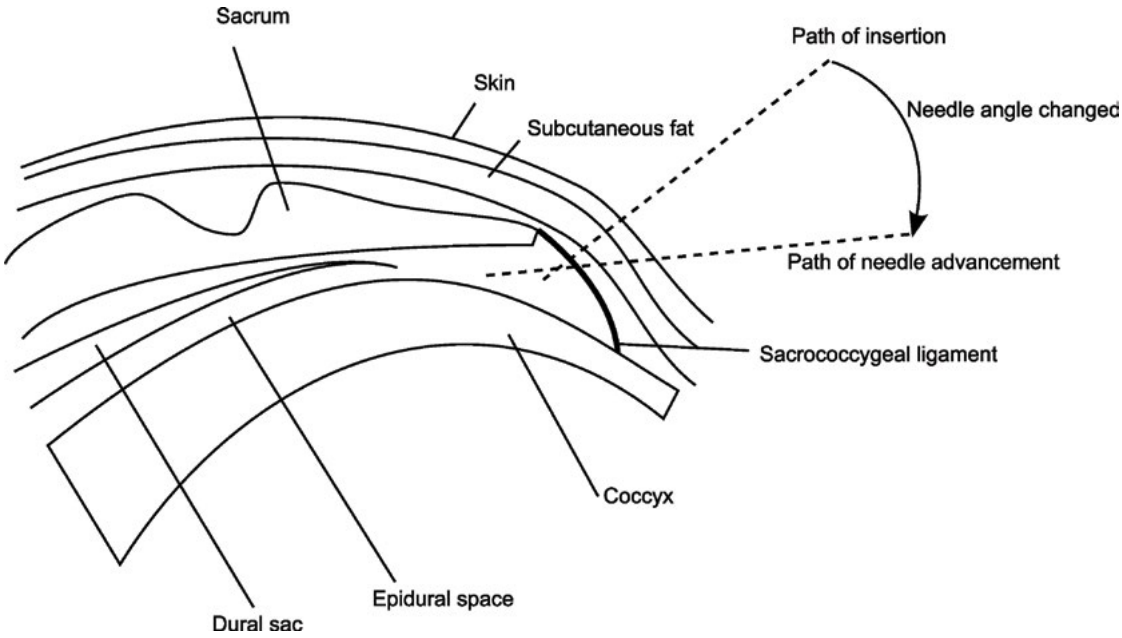

Figure 1. *Diagrammatic representation of needle insertion and advancement for caudal anaesthesia.*

abdominis. [6] These injections cover the ilioinguinal, iliohypogastric and lower intercostal nerves, anaesthetising the operating field, including the inguinal sac. [3] Commonly, these nerves are blocked by the surgeon during the surgical process when she/he can apply local anaesthesia directly to the nerves. Ultrasound guidance has enabled the more accurate placement of injections, allowing lower doses to be used [7] and improving success rates, [8] leading somewhat to a resurgence of the technique. [4]

Pharmacological aspects

Considerable discussion has arisen regarding which local anaesthetic agent is the best choice for caudal anaesthesia: bupivacaine or the newer pure left-isomers levobupivacaine and ropivacaine. A review by Casati and Putzu examined evidence regarding the toxicology and potency of these new agents in both animal and human studies. Despite conflicting results in the literature, this review ultimately suggests that there was a very small difference in potency between the agents: bupivacaine is slightly more potent than levobupivacaine, which is slightly more potent than ropivacaine. [9] Breschan et al. suggested that a caudal dose of 1 mL/kg of 0.2% levobupivacaine or ropivacaine produced less post-operative motor blockade than 1 mL/kg 0.2% bupivacaine. [10] This result could be consistent with a mild underdosing of the former two agents in light of their lesser potency, rather than intrinsic differences in motor effect. Doses for ilioinguinal nerve block are variable, given the blind technique commonly employed and the need to obtain adequate analgesia. Despite this, the maximum recommended single shot dose is the same for all three agents: neonates should not exceed 2 mg/kg, and children should not exceed 2.5 mg/kg. [11] Despite multiple studies showing minimal yet statistically significant differences, all three agents are nonetheless comparably effective local anaesthetic agents. [9]

When examining toxicity of the three agents discussed above, Casati and Putzu reported that the newer agents (ropivacaine and levobupivacaine) were less toxic than bupivacaine, resulting in higher plasma concentrations before the occurrence of signs of CNS toxicity, and with less cardiovascular toxicity occurring at levels that induce CNS toxicity. [9] Bozkurt et al. determined that a caudal dose of 0.5 mL/kg of 0.25% (effectively 1.25 mg/kg) bupivacaine or ropivacaine resulted in peak plasma concentrations of 46.8 ± 17.1 ng/mL and 61.2 ± 8.2 ng/mL, respectively. These are well below the levels at which toxic effects appear for bupivacaine and ropivacaine, at 250 ng/mL and 150-600 ng/mL, respectively. [12] The larger doses required for epidural anaesthesia and peripheral nerve blocks carry the increased risk of systemic toxicity, so the lesser toxic potential of levobupivacaine and ropivacaine justifies their use over bupivacaine. [9,13] However, partly due to cost bupivacaine remains in wide use today. [14]

Caudal anaesthesia requires consideration of two aspects of dose: concentration and volume. The volume of the injection controls the level to which anaesthesia occurs, as described by Armitage:

- 0.5 mL/kg will cover sacral dermatomes, suitable for circumcision
- 0.75mL/kg will cover inguinal dermatomes, suitable for inguinal herniotomy
- 1 mL/kg will cover up to T10, suitable for orchidopexy or umbilical herniotomy
- 1.25 mL/kg will cover up to mid-thoracic dermatomes. [15]

It is important to ensure both an adequate amount of local anaesthetic (mg/kg) and an adequate volume for injection (mL/kg) are used.

Efficacy of caudal and ilioinguinal blocks

Ilioinguinal block and caudal anaesthesia both provide excellent analgesia in the intraoperative and postoperative phases. Some authors suggest that ultrasound guidance in ilioinguinal block can increase accuracy of needle placement, allowing a smaller dose of local anaesthetic. [16] Thong et al. reviewed 82 cases of ilioinguinal block without ultrasonography, and found similar success rates to other regional techniques, [17] however, this was a small study. Markham et al. used cardiovascular response as a surrogate marker for intraoperative pain and found no difference between the two techniques. [18] Other studies have shown that both techniques provide similarly effective analgesic profiles in terms of post-operative pain scores, [19] duration or quality of post-operative analgesia, [20] and post-operative morphine requirements. [21]

Caudal anaesthesia has a success rate of up to 96%, [22] albeit with 25% of patients requiring more than one attempt. In contrast, blind ilioinguinal block has a success rate of approximately 72%. [23] Willschke et al. quoted success rates of 70-80%, which improved with ultrasound guidance. [16] In a small study combining the two techniques, Jagannathan et al. explored the role of ultrasound-guided ilioinguinal block after inguinal herniotomy surgery performed under general anaesthetic with caudal block. With groups randomised to receive injections of normal saline, or bupivacaine with adrenaline, they found that the addition of a guided nerve block at the end of the surgery significantly decreased post-operative pain scores for the bupivacaine with adrenaline group. [24] This suggests that the two techniques can be combined for post-operative analgesia. Ilioinguinal block is not suitable as the sole method of anaesthesia, as its success rate is highly variable and the block not sufficient for surgical anaesthesia, whereas caudal block can be used as an awake regional anaesthetic technique. Both techniques are suitable for analgesia in the paediatric inguinal herniotomy setting.

Complications and side effects

Complications of caudal anaesthesia are rare at 0.7 per 1000 cases. [5] However, some of these complications are serious and potentially fatal:

- accidental dural puncture, leading to high spinal block
- intravascular injection
- infection and epidural abscess formation
- epidural haematoma. [4,13]

A comprehensive review of 2,088 caudal anaesthesia cases identified 101 (4.8%) cases in which either the dura was punctured, significant bleeding occurred, or a blood vessel was penetrated. Upon detection of any of these complications, the procedure was ceased. [25] This is a relatively high incidence; however, these were situations where potentially serious complications were identified prior to damage being done by injecting the local anaesthetic. The actual risk of harm occurring is unknown, but is considered to be much lower than the incidence of these events. Polaner et al. reviewed 6011 single shot caudal blocks, and identified 172 (2.9%) adverse events, including eighteen positive test doses, five dural punctures, 38 vascular punctures, 71 abandoned blocks and 26 failed blocks. However, no serious complications were encountered as each of these adverse events were detected early and managed. [26] Methods of minimising the risk of these complications include test doses under ECG monitoring for inadvertent vascular injection (tachycardia will be seen) or monitoring the onset of subarachnoid injection (rapid anaesthesia will occur). [13]

Ilioinguinal blocks, as with all peripheral nerve blocks, are inherently less risky than central blockade. Potential complications include:

- infection and abscess formation
- mechanical damage to the nerves.

More serious complications identified at case-report level include cases of:

- retroperitoneal haematoma. [27]
- small bowel perforation. [28]
- large bowel perforation. [29]

Polaner et al. reviewed 737 ilioinguinal-iliohypogastric blocks, and found one adverse event (positive blood aspiration). [26] This low

morbidity rate was attributed to the widespread use of ultrasound guidance. [26]

A number of studies have examined the side effect profiles of both techniques:

- Time to first micturition has conflicting evidence – Markham et al. suggest delayed first micturition with caudal anaesthesia compared to inguinal block, [18] but others found no difference. [19,20]
- Post-operative time to ambulation is similar. [18,19]
- Post-operative vomiting has similar incidence, [18-20] and has been shown to be affected more by the accompanying method of general anaesthetic than the type of regional anaesthesia, with sevoflurane inhalation resulting in more post-operative vomiting than intravenous ketamine and propofol. [30]
- Time in recovery bay post-herniotomy was 45 ± 15 minutes for caudal, and 40 ± 9 minutes ($p<0.02$) for ilioinguinal; [19] however, this statistically significant result has little effect on clinical practice.
- Time to discharge (day surgery) was 176 ± 33 minutes for caudal block, and shorter for ilioinguinal block at 166 ± 26 minutes ($p<0.02$). [19] Again, these times are so similar as to have little practical effect.

These studies suggest that the techniques have similar side effect incidences and postoperative recovery profiles, and where differences exist, they are statistically but not clinically significant.

Use of general anaesthesia in combination with caudal anaesthesia or ilioinguinal block

A topic of special interest is whether awake regional, rather than general, anaesthesia should be used. Although the great majority of inguinal herniotomy is performed with general and regional anaesthesia, the increased risk of post-operative apnoea in neonates after general anaesthesia (particularly in ex-low birth weight and preterm neonates) is often cited. Awake regional anaesthesia is therefore touted as a safer alternative. As described above, ilioinguinal block is unsuitable for use as an awake technique, but awake caudal anaesthesia has been successfully described and practised. Geze et al. reported on performing awake caudal anaesthesia in low birth weight neonates and found that the technique was safe; [31] however, this study examined only fifteen cases and conclusions regarding safety drawn from such a small study are therefore limited. Other work in the area has also been limited by cohort size. [32-35] Lacrosse et al. noted the theoretical benefits of awake caudal anaesthesia for post-operative apnoea, but recognised that additional sedation is often necessary, and in a study of 98 patients, found that caudal block with light general anaesthesia using sevoflurane was comparable in terms of safety to caudal anaesthesia alone, and had the benefit of offering better surgical conditions. [36] Additionally, the ongoing concerns around neurotoxicity of general anaesthetic agents to the developing brain need further evaluation before recommendations can be made. [37] More research is needed to fully explore the role and safety of awake caudal anaesthesia, [38] and it currently remains a highly specialised area of practice, limited mainly to high risk infants. [39]

Adjuncts to local anaesthetics

There are many potential adjuncts for caudal anaesthesia, but ongoing concerns about their safety continue to limit their use. The effect of systemic opioid administration on the quality of caudal anaesthesia has been discussed in the literature. Somri et al. studied the administration of general anaesthesia and caudal block both with and without intravenous fentanyl, and measured plasma adrenaline and noradrenaline at induction, end of surgery and in recovery as a surrogate marker for pain and stress. They found adding intravenous fentanyl resulted in no differences in plasma noradrenaline, and significantly less plasma adrenaline only in recovery. [40] Somri et al. questioned the practical significance of the result for adrenaline, noting no clinical difference in terms of blood pressure, heart rate or end-tidal CO_2. Thus they suggested that general anaesthesia and caudal anaesthesia adequately block the stress response, and therefore there is no need for intraoperative fentanyl. [40] Interestingly, they also found no difference in post-operative analgesia requirements between the two groups. [40] Other authors noticed no difference in analgesia for caudal anaesthesia with or without intravenous fentanyl, and found a significant increase in post-operative nausea and vomiting with fentanyl. [41] Khosravi et al. found that pre-induction tramadol and general anaesthesia are slightly superior to general anaesthesia and ilioinguinal block for herniotomy post-operative pain relief, but suggested that the increased risk of nausea and vomiting outweighed the potential benefits. [42] Opioids have a limited role in caudal injection due to side effects, including respiratory depression, nausea, vomiting and urinary retention. [43] Both ilioinguinal block and caudal block are effective on their own, and that the routine inclusion of systemic opioids for regional techniques in inguinal herniotomy is unnecessary and potentially harmful. Adding opioids to the caudal injection has risks that outweigh the potential benefits. [44]

Ketamine, particularly the S enantiomer which is more potent and has a lower incidence of agitation and hallucinations than racemic ketamine, [44] has been studied as an adjuvant for caudal anaesthesia. Mosseti et al. reviewed multiple studies and found ketamine to increase the efficacy of caudal anaesthesia when combined with local anaesthetic compared to local anaesthetic alone. [44] Similar results were found for clonidine. [44] This is consistent with other work comparing caudal ropivacaine with either clonidine or fentanyl as adjuvants, which found clonidine has a superior side effect profile. [45] However, the use of caudal adjuvants has been limited due to concerns with potential neurotoxicity (reviewed by Jöhr and Berger). [4]

Local anaesthetic with adrenaline has been used to decrease the systemic absorption of short acting local anaesthetics and thus enhance the duration of blockade. Its sympathetic nervous effects are also useful for identifying inadvertent intravascular injection, which results in increased heart rate and increased systolic blood pressure. The advent of longer acting local anaesthetics has led to a decline in the use of adrenaline as an adjuvant to local anaesthetics, [44] and the validity of test doses of adrenaline has been called into doubt. [46]

Summary and Conclusion

Both caudal and ilioinguinal blocks are effective, safe techniques for inguinal herniotomy (Table 1). With these techniques there is no need

Table 1. *Summary of characteristics of ilioinguinal nerve block and caudal anaesthesia.*

	Ilioinguinal nerve block	Caudal anaesthesia
Advantages	• Simple • Quick • Reliable	• Reliable • Good anatomical landmarks • Easily learnt technique • Can be used as an awake technique
Disadvantages	• Risk of viscus puncture • Mechanical nerve damage • Variable success rate	• Unrecognised intravascular and intradural injections • Nerve injury • Haematoma • infection
Notes	• Improved success with ultrasound will redefine the role for ilioinguinal block	• Not suitable in setting of sepsis, coagulopathy, local skin infection • Highly expert area for awake techniques

for routine intravenous opioid analgesia, thus reducing the incidence of problems from these drugs in the postoperative period. The role of ultrasound guidance will continue to evolve, bringing new levels of safety and efficacy to ilioinguinal blocks. Light general anaesthesia with regional blockade is considered the first choice, with awake regional anaesthesia for herniotomy considered to be a highly specialised field reserved for a select group of patients. However, the ongoing concerns of neurotoxicity to the developing infant brain may fundamentally alter the neonatal anaesthesia landscape in the future.

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Conflict of interest

None declared.

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Rationalisation of cancer therapy: modelling the physical and immunological tumour microenvironment

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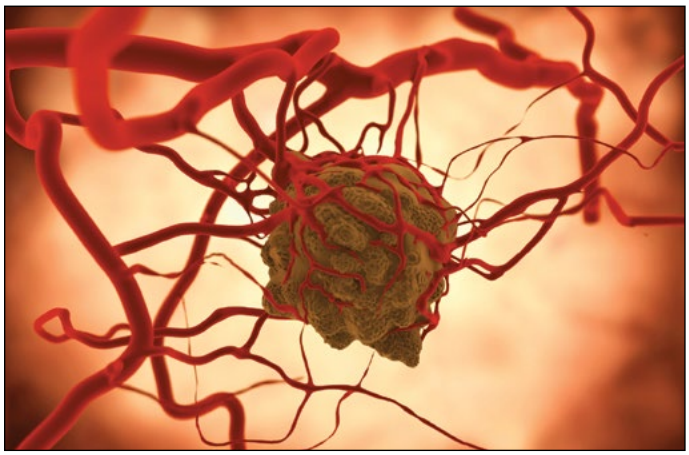
Kok-Ho's interest lies in infectious diseases and oncology; in particular, the use of microbial therapeutics in cancer treatment. Kok-Ho's primary motivation in medicine is to find a novel therapy for cancers with poor prognosis.

The tumour microenvironment has emerged as an important field in carcinogenesis. For most of the 20th century, cancer therapies have focused predominantly on tumour cells. Despite our best efforts, these therapies remain ineffective against cancers with poor prognosis such as ovarian and pancreatic cancer. Studies have shown that the tumour microenvironment consists of a variety of epithelial and stromal cells which interact with one another and influence the outcome of treatment. By considering these interactions within a microenvironmental model of carcinogenesis, it may be possible to optimise cancer treatment strategies using not only conventional methods such as chemotherapy and radiotherapy, but emerging methods such as gene therapy and immunotherapy. This article will attempt to briefly illustrate the potential of translating microenvironmental characteristics into clinical practice by using a specific model of carcinogenesis.



Introduction

In the 20th century, the somatic mutation theory has dominated our view of carcinogenesis. Cancer was viewed as a cellular phenomenon where genetic abnormalities result in aberrant cells that proliferate uncontrollably. [1,2] The theory, however, does not explain why certain cancers with known mutations (e.g. BRCA1/2 in breast cancer) only arise in a subset of patients; suggesting a role for non-genetic factors. [3] Thus, the tumour microenvironment is increasingly recognised as an important determinant of cancer progression.

In this environment, tumour cells co-exist with stromal cells such as fibroblasts and immune cells. Immune cells were first implicated in carcinogenesis by Virchow in the 19th century when he observed that leucocytes infiltrate into neoplasms and these sites of infiltration often correlated with chronic inflammation. [4] This inflammation is associated with autoimmune diseases (e.g. inflammatory bowel disease in colorectal cancer) and infections (e.g. *Helicobacter pylori* in gastric cancer) and generally involves tumour-promoting immune cells such as regulatory T-cells (Tregs), immature dendritic cells (DCs) and M2-polarized tumour-associated macrophages (TAMs). [5] Conversely, Fehleisen and Bruns found that acute inflammation had a tumour-suppressive effect. This was based on experiments whereby acute infections (e.g. erysipelas) of cancer wounds often resulted in tumour regression; [6,7] mediated in part by immune cells such as natural killer (NK) cells, CD8+ T cells (CTLs) and M1-polarized macrophages. [5] These two groups of immune cells differ in their cytokine profile. For example, M1 macrophages tend to produce pro-inflammatory cytokines such as interleukin-6 (IL-6), IL-12 and IL-23 which impede tumour progression while M2 macrophages produce anti-inflammatory cytokines such as IL-4, IL-10 and IL-13 which promote tumour progression. [8]

Tumour-associated fibroblasts are also associated with carcinogenesis. They originate predominantly from the mesenchyme and can produce matrix metalloproteinases (MMPs) which degrade the extracellular matrix (ECM) and enable invasion of cancer cells. [9] Furthermore, fibroblasts are a potent source of growth factors such as vascular endothelial growth factor-A (VEGFA) which promote angiogenesis. [9]

In tumourigenesis, the vasculature can also be leaky and malformed; resulting in the formation of hypoxic and acidic regions due to a lack of oxygen perfusion and a subsequent switch to anaerobic respiration. [10] Dysfunctional lymphatic vessels also significantly increase the interstitial fluid pressure within the ECM, thus impeding the entry of chemotherapeutic drugs by transcapillary flow and convection. [11] As these drugs are also oxygen or pH sensitive (e.g. doxorubicin), the efficacy of chemotherapy is severely limited.

To understand the role of the tumour microenvironment in carcinogenesis, it is essential to visualise its features in the context of a model. It is important to note, however, that this article is not comprehensive; rather it is meant to highlight points of interest for further reading.

Developing a microenvironmental model of carcinogenesis

A multistep model for carcinogenesis was proposed by Fearon and Vogelstein in 1990. Based on observations documented in human colorectal cancer, they linked changes in tumour morphology to specific mutations in oncogenes and tumour suppressor genes. [12] They proposed that accumulation of mutations, rather than sequence, was seen as the most important determinant of tumour progression. [12] In 2000, Hanahan and Weinberg proposed that six acquired traits are required for the formation of an invasive cancer. These include: self sufficiency of growth signals, insensitivity to anti-growth signals, resistance to apoptosis, unlimited replication, sustained angiogenesis and invasiveness. [13]

Subsequently, studies have shown that the microenvironment can affect the development of cancer cells. [14] Fuelled by the tissue organisation field theory (TOFT), it was believed that tissue homeostasis is controlled by stroma-epithelium interactions that impose environmental barriers to tumour progression. [15] During tumourigenesis, such barriers go awry and affect the type and sequence of phenotypic strategies adopted by cancer cells (that is, observable characteristics manifested by cancer cells to override barriers). [16]

Finally, in 2007, Gatenby and Gilles proposed a sequential microenvironmental model. [16] In this model, the initiating event is insensitivity to anti-growth signals mediated by contact inhibition (arrest of growth by cell contact). [17] Tumour cells escaping from the basement membrane (BM) survive by up-regulating growth factors and/or their receptors to acquire self-sufficiency; illustrating the ability

of tumour cells to contribute to signals in the microenvironment [18,19] As proliferation occurs, tumour cells are constantly constrained by senescence (through cellular ageing by telomere shortening) and therefore require increased telomerase activity to avoid apoptosis. [20] Conditions become more hypoxic in distal regions of the tumour and distal cells adapt by switching to glycolysis and increasing glucose uptake. [21] This altered metabolism results in a low extracellular pH which is toxic to tumour cells. To counter this situation, cells may acquire p53 mutations or increase Na^+/H^+ exchanger activity. [16] Alternatively, transcription factor hypoxia-inducible factor 1 (HIF-1) may be up-regulated in response to hypoxia, resulting in a gene expression profile (for example VEGF and glycolytic factors) which overcomes both hypoxia and acidosis. [22]

Despite these strategies, the poorly formed vasculature is usually unable to match the tumour's demand and nutrients need to be supplied by angiogenesis. [23] Increasingly unfavourable conditions eventually promote tumour cells to be invasive by favouring motile cells which can spread to adjacent normal tissue.

The abbreviated development of a microenvironmental model is summarised in Figure 1.

From the Gatenby and Gilles model, several principles can be extrapolated. [16] First, carcinogenesis can be viewed as a sequence of phenotypic strategies selected by conditions in the microenvironment. Second, different phenotypic strategies can be utilised by the tumour as long as they confer the same selective advantage towards overcoming unfavourable environmental conditions. Third, phenotypic strategies at a particular stage of tumourigenesis may impede or promote progression through subsequent environmental barriers.

Targeting the tumour microenvironment

If carcinogenesis progresses in a sequential manner, appropriate treatment can be initiated at specific stages of progression. Withstanding the variability of different cancers, the Gatenby and Gilles model offers good insights by proposing one of many possible progression sequences. The challenge to this phenotype-specific approach lies in the ability to model the different cancer microenvironments and the prompt detection of cancerous changes; many cancers (for example, gastric cancer) are not detected at the early stages of disease. [24] Recent advances in molecular and mechanical characterisation methods have been encouraging. Using a proteomics approach, Ryu et al. have identified two groups of proteins which are over-expressed (for example, transgelin and prohibition) and under-expressed (for example, desmin and serotransferrin) in gastric cancer while Vakoc et al. have developed an advanced form of three-dimensional microscopy known as optical frequency domain imaging (OFDI) which is capable of investigating huge tissue volumes and dynamic tumour changes over long periods. [25,26]

Targeting inflammation as a sequential entity

The sequential transition of acute to chronic inflammation may be involved in tumour progression. Cancer and infections, autoimmunity and graft rejection share biphasic patterns characterised by waxing and waning of immune responses. [27] These patterns may be attributed to a common immunological constant of rejection. Mantovani et al. hypothesised that inflammation can be divided into two tiers. The first tier is thought to be a baseline level of inflammation mediated by activation of interferon-stimulated genes (ISGs). [28] This was based on experimental evidence showing a convergence of ISG expression in cancer and chronic states such as persistent hepatitis C virus (HCV) infections and long-term transplant rejections treated with immunosuppressants. [29] Conversely, the second tier is a cytotoxic-mediated inflammation provided by CTLs and NK cells. This is more commonly seen in tumour regression, acute exacerbations of inflammatory bowel diseases and acute hepatitis C-mediated liver cirrhosis. [27]

From Mantovani's hypothesis, two possible directions can be pursued: controlling the chronic baseline level of inflammation or promoting the cytotoxic effector functions of immune cells. Controlling chronic inflammation may be achieved by treating the underlying trigger such as infections (for example, HCV in hepatitis C and *Helicobacter pylori* in gastric carcinoma) or prevention using anti-inflammatory drugs. [30] The use of non-steroidal anti-inflammatory drugs (NSAIDs) has been associated with regression of established tumours or inhibition of pre-malignant lesions in cancers such as gastric and colorectal cancers. [31]

Targeting immune cells: enhancing cytotoxicity via innate immunity

Promoting the cytotoxic function of immune cells would require overcoming tumour-induced immunosuppressive networks (for example, Tregs and suppressive cytokines). Vaccination strategies involving tumour antigens and *ex vivo* activated T cells have been used to stimulate localised anti-tumour responses but results are

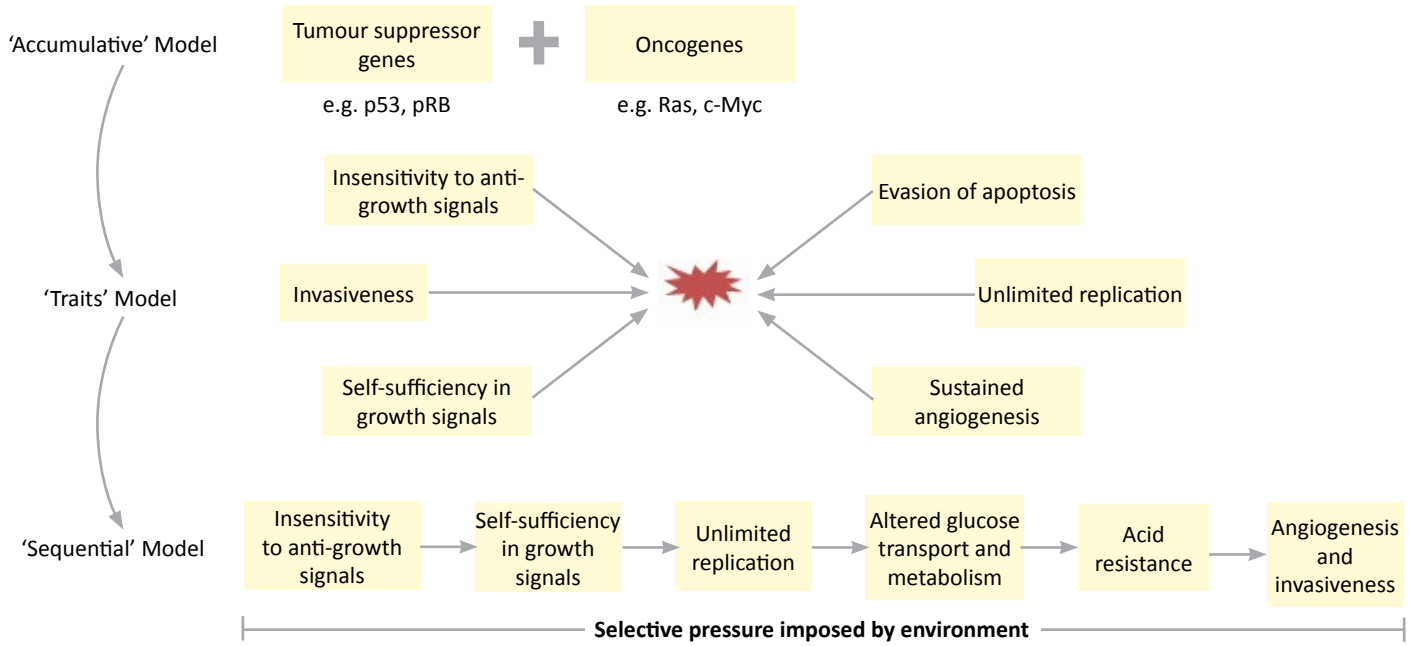


Figure 1. *Developing a microenvironmental model. Early researchers focused on the accumulation of TSGs (for example, p53 and pRB) and oncogenes (for example, Ras and c-Myc) as the driver for carcinogenesis. This was later replaced by an emphasis on understanding the different traits required for tumour survival. Growing recognition of the tumour microenvironment will necessitate a sequential model driven by selective pressures imposed by environmental barriers.*

disappointing because the role of innate immunity in shaping adaptive immune response has been neglected. [32] Effective CTL response requires co-stimulatory molecules. These molecules are up-regulated in response to pathogen-associated molecular patterns (PAMPs, such as lipopolysaccharides) interacting with toll-like receptors present in innate immune cells (such as DCs and macrophages). [33] It has been shown that interaction of TLR9 with CpG oligodeoxynucleotides results in high levels of anti-tumour interferon alpha (IFN-α) production while TLR7 agonists have been used to treat basal cell carcinoma via an IFN-γ mediated mechanism. [34,35] However, as some TLRs (namely TLR2 and TLR4) are also involved in chronic inflammation, TLR antagonists have been increasingly researched as potential anti-cancer agents. [36] A recent study also showed that a subset of DCs known as interferon-producing killer DCs can combine antigen-presenting and cytotoxic functions; suggesting that innate cells have an understated importance in tumour suppression. [37]

The importance of innate cells is further illustrated by NK cells. Natural Killer cells function as an important link between innate and adaptive immunity as they are involved in DC maturation which then facilitates priming of effective CTL responses. [38] Illustrating the third principle, tumours are shown to reduce major histocompatibility complex (MHC) Class I expression as a means of evading CTLs and this renders them sensitive to NK cell-mediated cytotoxicity [39]. Nonetheless, low NK cell count in tumours (due to lack of chemokines or proliferative cytokines) may explain why tumours continue to progress. Studies have shown that intratumoural injection of CpG oligodeoxynucleotides can improve NK cell infiltration while Treg depletion followed by IL-15/hydrocortisone induction significantly induced higher NK cell numbers. [40,41] Similarly, induced pluripotent stem cell (IPSC) derived NK cells have been shown have a positive effect on tumour regression in several cancers. [42,43] These observations suggest that NK cell-based immunotherapy can be effective.

Targeting single cytokines or cells involved in cytokine networks?

To date, only two cytokines have been approved for cancer treatment: IL-2 and IFN-α. [44] IL-2 was initially tested in the 1980s a means of treating advanced solid cancers. It is worth postulating that their efficacy probably lies in some cancers exhibiting limited phenotypic strategies; thereby explaining why few cytokines have been approved. [45] Although a favourable response was found in renal cell carcinoma patients, efficacy was limited at 30% while IL-2 was implicated in the potentially fatal capillary leak syndrome. [46] Furthermore, IL-2 used to expand CTL subsets was also found to increase Treg numbers; effectively down-regulating the initial cytotoxic response. [47] Inhibition of cytokines implicated in tumourigenesis (such as IL-6) by monoclonal antibodies has also been considered but this approach has been largely limited as IL-6 receptors are not tumour-specific. Tumours have complex cytokine networks; these cytokines work in tandem and cancers may exploit multiple cytokines to achieve progression. [48] Limiting one arm of this network may simply activate another; thus requiring us to consider cytokine therapy on an integrative level.

Targeting cells involved in cytokine networks may achieve the same effect as administering multiple cytokines. For example, two potential targets for TAMs include the interferon response factor 5 (IRF5) and the Src homology 2 domain-containing inositol-5-phosphatase 1 (SHIP1). Interferon response factor 5 is a transcription factor that is involved in M1 phenotype polarization (high levels of IL-12 and IL-23, low levels of IL-10). [49] The other target SHIP1 is a phosphatase that is also involved in M1 macrophage polarization and is a potent repressor of M2 polarization. [50] Experiments demonstrated that mice deficient in SHIP1 not only develop M2 phenotype macrophages but also have a higher incidence of tumour formation. [50] Both IRF5 and SHIP1 may potentially be targeted by gene silencing techniques (such as RNA interference) in the future. [51]

Targeting the physical environment: The example of HIF-1

Hypoxic strategies may underlie the importance of an integrated treatment approach in targeting multiple phenotypic strategies. Low oxygen content can result in tumour cells that adapt by inducing HIF-1 expression. This leads to reduction in oxygen consumption by the mitochondria as well as increased transport and anaerobic metabolism of glucose. [52] In response to HIF-1, vascular endothelial growth factor (VEGF) may also be up-regulated in the tumour microenvironment to improve oxygenation by angiogenesis. [53] Anti-VEGF agents such as bevacizumab were initially used to inhibit angiogenesis in colorectal cancer but researchers later realised that it may normalise tumour vasculature and paradoxically lead to higher oxygen levels and increased risk of metastasis. [52] Although oxygenation potentially improves radiotherapy and oxygen-dependent chemotherapeutic drugs like etoposide and mephalan, there may be a trade-off between improving short-term outcomes at the expense of tumour persistence. [54] It has been postulated that cancer stem cells (CSCs) may be found proximal to blood vessels. [55] CSCs are tumourigenic cancer cells capable of self-renewal and differentiation into all cancer cell types and are refractory to many forms of chemotherapy; promoting survival of these cells therefore predisposes to cancer regeneration. [56] Multiple phenotypic strategies can be targeted specifically to restrain tumour cells from exploiting alternate pathways. Where possible, targeting a pleiotropic transcription factor such as HIF-1 by inhibitors such as phenethyl isothiocyanate (by translation inhibition) may achieve the same outcome as targeting multiple strategies. [57] This is because HIF-1 trans-activates many genes involved in the tumour's phenotypic strategies (including VEGF, mitochondrial regulators and glycolytic enzymes). [22]

The third principle states that phenotypic strategies may have paradoxical effects on tumour progression. While HIF-1 leads to a switch to glycolysis and also helps overcome acidosis and ischaemia, other phenotypic strategies may increase the threshold for future barriers. [16] The initial phenotypic strategy of avoiding cell death after BM detachment permits distal cell proliferation but consequently, subsequent 'thresholds' of environmental barriers are increased as highlighted by higher degrees of growth signal insufficiency and hypoxia that impede distal tumour cells. [16]

These observations have implications for treatment. First, strategies that lower the threshold for subsequent barriers should be actively targeted since they may hasten the progression of malignancy. Second, strategies that increase the threshold may result in low to mid-grade malignancies that are amendable to our current conventional approach. For example, basal cell carcinoma is typically a low-grade malignancy that is highly responsive to radiotherapy and surgical excision. [58]. These observations may suggest why early-stage neoplasms tend to have a favourable prognosis, whereas late-stage malignancies probably exhibit features of threshold reducing strategies and are thus more aggressive.

Further considerations: Combination therapies and multiple microenvironmental 'niches'

The vast array of components in the tumour microenvironment not only highlights the importance of integrative treatment but also the need for combination therapies focusing on multiple treatment modalities. The latter may be relevant to highly resistant cancers that are likely to exhibit phenotypic strategies that reduce the threshold of environmental barriers. An example of combination therapy is the use of low-dosage cyclophosphamide with dendritic cell-based immunotherapy in mesothelioma. [59] While mesothelioma is generally resistant to most cytotoxic chemotherapeutic drugs such as cisplatin and docetaxel, low-dosage cyclophosphamide can potentiate the immune-stimulatory effects of DC vaccination via inhibition of Tregs. [60] Thus, combination therapies can essentially bypass the ability of cancers to circumvent some environmental barriers by increasing the threshold of other barriers.

Tumour progression is also a dynamic process and when considering the microenvironment in invasive cancers, this is in reality a combination

of different unique 'niches' composing of primary and metastatic sites. [61] This will inadvertently complicate the treatment process due to heterogeneity of different tumour environments but it is reasonable to assume that targeting the primary site will still be of important therapeutic value due to the role of the primary tumour in 'seeding' metastases and also possible parallel progression of primary tumours and metastases. [62]

Based on all three principles and the examples highlighted, rational treatment strategies may be designed (Figure 2).

Conclusion

In 2008, it is estimated that almost 7.6 million deaths were attributed to cancer. [63] Almost one in two patients treated for invasive cancer eventually succumb to the disease or the treatment. [64] As such, the design of current treatment strategies may be further improved to reduce mortality rates.

The medical practitioners of tomorrow will be given new tools in the fight against cancer. It is against this backdrop that devising rational treatment strategies becomes essential. The examples described suggest the importance of tumour characterisation and tailoring different approaches to these characteristics. Although this review only focused on a single model and specific examples, there can be more than one model of carcinogenesis for different cancers and many more treatment targets are under consideration.

The challenge to devising a good treatment strategy would be selecting the appropriate target(s) and considering the need for integrative/combination or conventional single-modality approaches. In particular, combining different treatment modalities may be crucial for persistent cancers and should be the focus of current research.

Conflict of interest

None declared.

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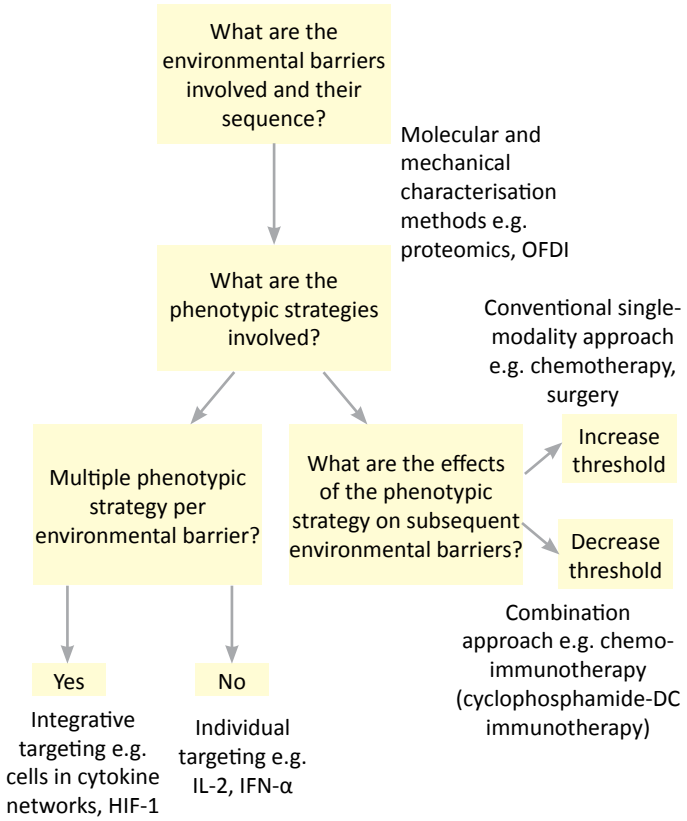

Figure 2. *Devising rational cancer treatment strategies Molecular and mechanical characterisation methods can be used to determine environmental barriers and their corresponding tumour phenotypic strategies. Integrative targeting (for example, cytokine networks) may be useful against multiple phenotypic strategies while individual targeting (for example, single cytokines) may favour cancers with limited strategies. The effect of phenotypic strategies on the level of threshold may also determine the type of treatment approach-single modality for increased threshold and combination for decreased thresholds.*

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The benefits associated with male HPV vaccination in Australia

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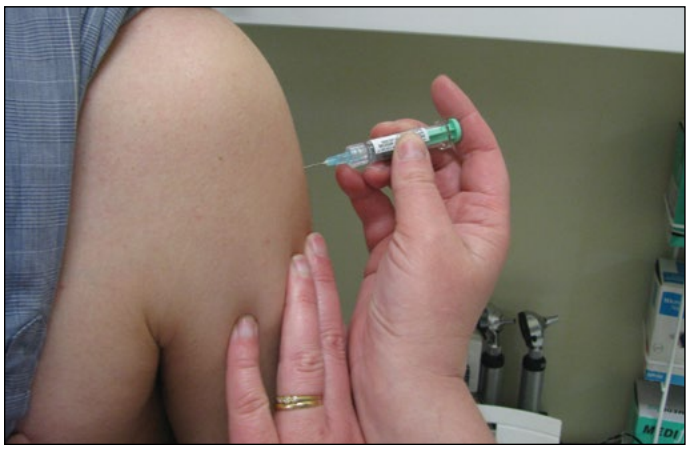
Background: Human papillomavirus (HPV) is a family of highly contagious sexually transmitted viruses which are associated with the development of genital warts and certain HPV related cancers in males and females. After conducting a cost-effective analysis, the Australian Government has decided to expand the school based female only HPV vaccination program to include males commencing in 2013. **Methods:** A search of Ovid MEDLINE, The Cochrane Library, Google Scholar, BMJ Journals, and JSTOR was undertaken. **Discussion:** HPV vaccination has proven to have a high safety profile with sustained efficacy rates. Male vaccination will not only offer immunity to its recipients but also provide indirect protection to both sexes and high risk groups through herd immunity. The included high risk HPV strains 16 and 18 are associated with more than 70% of cervical cancers, 80% of anal cancers, 25% of penile cancers and 31% of oropharyngeal cancers worldwide. The quadrivalent vaccine also covers HPV 6 and 11 which are responsible for 90% of genital warts. **Conclusion:** Robust monitoring and surveillance systems are in place which will enable Australia to quantify the impacts of HPV vaccination in the future. Models show that the rates of HPV infection will further reduce by an additional 24% in 2050 compared to female vaccination alone, if vaccination rates for boys reach the same levels attained by girls in 2011. This will result in a significant decrease in the clinical burden of HPV-related diseases, the associated costs of treatment, and the psychological trauma which often accompanies the diagnosis of an HPV-related condition.

Introduction

Human papillomavirus (HPV) is a highly contagious family of viruses with over 150 distinct genotypes. [1] The virus infects the squamous epithelium in both males and females, with over 40 genotypes affecting the anogenital region. [2-4] HPV is usually a transient, asymptomatic infection which is transmitted through skin-to-skin contact associated with sexual activity, and the risk of infection increases with a greater number of sexual partners. [2-5] HPV is also the most common sexually transmitted infection (STI), [6] with up to 80% of people being infected with at least one type of genital HPV in their lifetime. [3,7,8]

There is a proven association establishing the relationship between persistent HPV infection and the development of pre-cancerous (CIN) and cancerous lesions in females. [7] Australia was the first of many countries to create a National HPV Vaccination Program for females, and has been providing the school based HPV vaccination to 12-13 year old girls since 2007. [9,10] Males are expected to join their female counterparts commencing in February 2013. [11,12]

Australia provides this vaccination in the form of the quadrivalent Gardasil® vaccine which covers four types of HPV (6, 11, 16 and 18). [8] In women, although there are many 'high risk' types, HPV 16 and 18 alone are associated with 70% of cervical cancers, [2,3,13] and 32% of vaginal cancers worldwide. [14] In men and women, those two types also contribute to over 80% of anal cancers, 24% of oral cancers, and 31% of oropharyngeal cancers. [6,14] Furthermore HPV 16 and 18



account for 90% of all HPV attributable male cancers. [5]

The other two HPV types covered by the quadrivalent vaccine, HPV 6 and 11, are associated with 90% of genital warts and 100% of juvenile onset recurrent respiratory papillomatosis (RRP) cases, resulting in a severe respiratory condition. [14] Recent studies also reveal that more than 4% of all cancers worldwide may be caused by HPV. [15,16]

On the back of such evidence, the Australian Government has announced the introduction of the quadrivalent HPV vaccination for males in the 12 -13 age group, with a catch-up program for males aged 14-15 years at school. [11,12] Early data show that 73% of females in the 12-13 age group received the full course of three doses (Figure 1). This level of coverage is significantly higher than the levels in the catch up programs where the lowest level is 30% in the 20-26 year old age group. Therefore, introducing an immunisation program for boys

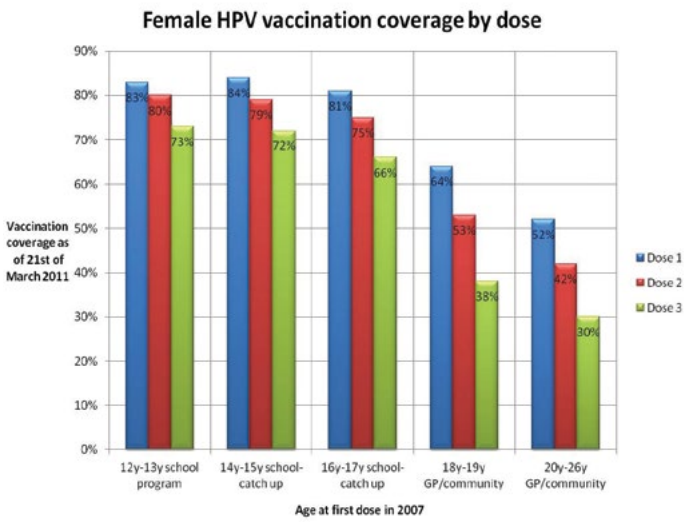


Figure 1. *A graphical representation of female vaccination coverage categorised into various target age groups in the 2007 HPV vaccination cohort. Raw data sourced from the Immunise Australia Program. [17]*

is a significant move towards preventing the many HPV attributable cancers and genital warts by accelerating coverage and the levels of herd immunity against HPV.

Therefore, the aim of this article is to examine the evidence which exists globally in supporting HPV vaccination and to identify any additional benefits routine male vaccination may provide. The article will also consider high risk population groups, the cost effectiveness of widespread HPV vaccination and the long term monitoring goals for the Australian vaccination program.

Methods

The review of the literature was undertaken through a search of Ovid MEDLINE, The Cochrane Library, Google Scholar, BMJ Journals, and JSTOR. The search aimed to find original research articles, reviews, case studies, and opinion pieces that related to HPV vaccinations and the spread of sexually transmitted infections. The terms used in our search ensured we reviewed a broad range of relevant studies. These terms were: 'human papilloma virus', 'males', 'quadrivalent', 'vaccine', 'sexually transmitted disease', 'cervical cancer', 'penile carcinoma', 'herd immunity', 'genital warts', 'cost effectiveness' and 'pap smear'. We also sought to review the 'grey literature', and therefore searched a broad range of internet sources, including government websites. These were accessed for up-to-date information on the HPV vaccination program, the cervical screening program, and relevant legislation. The studies were limited to those published in the English language after the year 2000.

Using the methodology described above, 63 articles and documents found during the search were selected for consideration. After individually analysing all the identified documents, 39 publications were selected for inclusion in the final review with preference given to more recent publications and those with data which could be applied to the Australian program. Of these remaining publications, 16 were original research articles, 15 were review articles, 6 were Australian Government reports or legislation, 1 was a professional communication, and 1 was a media release. The remaining 24 publications were excluded as they were assessed as not relevant to the Australian program.

Discussion

Evidence for HPV vaccination in men

HPV vaccinations worldwide has revealed no major safety concerns, [5] and recent clinical trial data show that the safety profile for males is the same as for females. [18] The most commonly reported side effects have been mild and include fever, nausea and localised injection site pain. [19] Furthermore, there have been no reported deaths that are directly attributable to the vaccine. [5,20]

Currently, only the quadrivalent vaccine has demonstrated protective effects for males in clinical trials. [18] Boys vaccinated with the quadrivalent vaccine have the same seroconversion rates as girls, which is as high at 99%. [21] In addition, the current implementation of the HPV vaccination program for girls in Australia does not have full coverage. [8] Vaccinating males will provide indirect protection to the targeted females in the school HPV vaccination program who were not fully vaccinated, by increasing herd immunity. [8] This protection is vital because there is good evidence that vaccines which include HPV 16 and 18 prevent persistent HPV infections and precancerous cervical, vulvar, and vaginal lesions in females. [14]

Therefore, the inclusion of males into the HPV vaccination program will provide them, and possibly their unvaccinated sexual partners, with protection from HPV. [14] This will also result in higher levels of herd immunity, which refers to the protective effect offered to the unvaccinated and susceptible population by having high rates of acquired immunity in the vaccinated population. [22] This phenomenon acts to limit the cases of transmission and the reservoirs of disease. One example of herd immunity is the widespread vaccination of males against rubella even though the virus is of little clinical significance in males. This vaccination program in Australia has led to a significant reduction in the transmission of rubella to susceptible pregnant females and the subsequent development of congenital rubella syndrome. [6,23]

Male vaccination not only provides direct protection to its recipients, it also further reduces rates of transmission [5] and provides indirect population benefits to protect members of both sexes through herd immunity. [24] A retrospective seminal study across Australia compared rates of genital warts before and after female vaccination and post immunisation in the 2004-2009 time period. Results demonstrated a 59% decrease in genital warts in age matched females who were eligible for free vaccination and a corresponding decrease of 28% in heterosexual males in the same age bracket who were ineligible for free vaccination. [25] These trends were supported by another Melbourne study which reported the near disappearance of genital warts in heterosexual females and males under 21 years of age. [26] These studies provide early evidence of the benefits of vaccination providing herd immunity which has reduced the clinical burden of genital warts, the high costs of treatment, [27] and the psychological impact associated with the condition. [28,29]

However, the impact of genital warts in the Australian community can be further reduced. One model of HPV transmission suggests that if vaccination rates for boys reached the same 73% level attained by girls in 2011, then by 2050 the vaccination of boys would have prevented an additional 24% of new HPV infections. [5] Other mathematical models suggest that while vaccination of 12 year old girls alone would reduce the incidence of genital warts by 83% and cervical cancer by 78%, including boys in the vaccination program would reduce the incidence of genital warts by 97% and cervical cancer by 91%. [30]

The vaccination of males would not only help the female population, but would also reduce the disease burden for males. This was demonstrated in study of 4065 healthy boys which demonstrated a clear reduction in the development of external genital lesions. [18] One month after the boys received their third and final vaccination, seroconversion for all four types of HPV had occurred in 97.4% of boys, with an additional 1.5% of the cohort seroconverting for only three types of the four. [18] Vaccination was shown to reduce the incidence of external genital lesions, due to infection with HPV types 6, 11, 16 and 18, by 90.4% in the per-protocol population. [18]

Nonetheless, the lack of long term data means there is currently no clinical evidence demonstrating a reduction in HPV related male cancers after vaccination. However, two of the quadrivalent vaccine types, HPV16 and HPV18, are responsible for 90% of all HPV attributable cancers in men. [5] Therefore, since the quadrivalent vaccine has demonstrated a reduction in high grade cervical lesions in women, [8] there is an expectation that vaccination will have the same effect for cancers in men. [8,31] Worldwide, HPV types 16 and 18 are associated with over 80% of anal cancers, 25% of penile cancers [6,14,15] and 31% of oropharangeal cancers, [14] so the potential for benefit is significant.

In addition, with the reduced rates of smoking, HPV is becoming an increasingly significant cause of oropharyngeal cancer. [32] Most of the oropharyngeal cancers in non-smokers are caused by HPV infections, and the majority of patients are men. [32] Vaccinating women alone is less effective in reducing the rates of infection and both males and females need to be vaccinated for maximal benefit. [22] Male HPV vaccination is expected to lead to a reduction in the oncogenic HPV prevalence in the community and together with female HPV vaccination, it may reduce the incidence of HPV related oropharyngeal cancers in non-smokers. [32]

However, the lack of long term data means that it is uncertain how long immunity will last before a booster is necessary. Current follow-up studies suggest that the vaccine remains effective in a population

vaccinated 8.5 years ago. [8] Further follow-up is necessary to ensure that the vaccine continues to be effective over longer periods of time.

Populations at risk

There is poor uptake of the National Cervical Screening program among women of Aboriginal and Torres Strait Islander (ATSI) background. [7] Among other factors, this poor uptake is one of the reasons why they have twice the risk of developing cervical cancer and their mortality rate is 5 times higher than the general population. [7]

Including boys in the vaccination program has been modelled to further decrease the rates of genital warts and cervical cancer beyond that which would be attained by female vaccination alone. [30] However, the argument has been made that if there is sufficient uptake of vaccination among girls most males would eventually be protected through female vaccination alone. [22] This argument has merit if the vaccination rates among girls are extremely high, but it assumes transmission only through heterosexual relationships. One of the populations at highest risk of HPV infection is men who have sex with men (MSM). [5] This population acquires little benefit from the current HPV vaccination program, [5] and logic suggests that the HPV infections would persist in this population even with immunisation of all females. MSM are at 30 times the risk of anal cancer when compared with other men. [5] As 90% of anal cancers are associated with HPV, [6] the vaccine has the potential to provide significant benefits for this high risk population. However, it would be difficult on many levels to target the MSM population for immunisation. Targeted immunisation would need to reach MSM at an early stage of sexual activity, but at that time many may be reluctant to disclose their sexual orientation due to a fear of stigma. [5] Therefore, a program of routine male vaccination solves the need to target this group specifically by immunising all young boys prior to sexual debut.

Another population which is at higher risk of HPV infection is men and women with impaired immunity such as organ transplant recipients. [6] Although heterosexual males with impaired immunity may have some protection from the HPV vaccination program for girls, [5,30] heterosexual females and MSM with impaired immunity would not receive the same degree of protection. Immunosuppressed populations are more likely to develop persistent infections which progress to dysplasia and cancer. [6] Wide vaccine coverage would ensure high levels of immunity in the community that should lower the risk of HPV transmission to all high risk groups.

Cost effectiveness

The immediate costs of implementing and monitoring the female-only HPV program was reported in 2007 to be AU$103.5 million over five years. [33] The addition of males to the program added AU$21.1 million over four years in 2012. [12] Although the Australian Government has approved the addition of males to the HPV vaccination program, the cost effectiveness of such a move is still debated in Australia and worldwide. [5,14,34,35]

Some studies have reported that the vaccination of males is not cost effective when compared to female vaccination alone. [5,14,34,35] These reports were made with the commonly used consideration that an incremental cost-effectiveness ratio (ICER) of greater than US$50,000 per quality-adjusted life-year (QALY) is not considered cost-effective. [5] However, other studies have shown that the equation becomes much more favourable when protection against all HPV related diseases affecting men and women are included, as that drops the ICER to US$25,664 per QALY. [36]

Although the Australian Government has not released their analysis on the cost effectiveness of including males in the HPV vaccination program, past experience suggests that anything below an ICER of less than AU$60,000 per QALY is generally accepted. [5]

The cost models can only provide an estimation of the impact of HPV vaccination and the true benefits of the HPV vaccination program will not be apparent for some time. This is due to the time interval between HPV infection and the development of cancer. [3,36] However, the rates of genital warts, which are more prevalent and develop more quickly, are already decreasing. [25,26]

The cost per person of vaccination may seem high initially but when the cumulative effects of herd immunity are taken in to account the equation becomes more favourable. [24] In addition, the benefits of HPV vaccination are many, and cost effectiveness studies should take into account the psychosocial benefit, the reduction in the clinical burden of disease, as well as the reduced costs of treating the various presentations of HPV related cancers and genital warts. For example, the treatment of genital warts alone is estimated to cost AU$14 million annually in Australia. [27]

Future research and monitoring

Monitoring the efficacy, safety and the impact of HPV vaccination is an important step in measuring the effectiveness of the vaccination program and in guiding future policy. There are some challenges in vaccine program monitoring due to the long time interval between HPV infection and the development of HPV related cancers, as well as the asymptomatic and transient nature of infection. [3,37] However, the setup of the National HPV Vaccine Program Register (NHVPR) is a key step towards collecting vaccine coverage and dose status data of the target population, as well as collecting basic demographic data of recipients across Australia. [33] This information is only collected with prior consent and enables administrators to match accurate data collected from different registers to individuals. This allows them to run follow up programs to send reminders for missed doses or for boosters if they are required in the future. These data, combined with the information collected by state based cervical cytology registers and the Australasian Association of Cancer Registries provides a powerful tool to quantify the impact of the vaccination program on the incidence of cervical and other HPV related cancers in the long term.

Information regarding the safety of the vaccine and any associated adverse effects is collected by the Medicines Safety Monitoring office of the Therapeutic Goods Administration. [20] However, currently there are no nationally funded programs which monitor HPV genotypes in the general population and the vaccinated group. This could be a method to monitor HPV prevalence in the future or a way to screen for HPV related cancers. [7] The impact of vaccination on targeted groups such as MSM and ATSI Australians should also be monitored to evaluate the impact of the prophylactic vaccine on these high risk groups.

Summary

The aim of the Australian immunisation program is to introduce immunity against the included HPV types before the commencement of sexual activity through a prophylactic HPV vaccine. Through this program, males and females in the pre-adolescent age group are immunised before their sexual debut (which usually creates a peak in incidence of HPV). [38]

Although the use of barrier contraception such as condoms, and male circumcision may offer some protection, any skin-to-skin contact during sexual activity can result in the transmission of HPV. [3] Currently, HPV vaccination is the only reliable and realistic method of primary prevention of HPV infection. It has proven to be safe with a high efficacy and minimal side effects. [20,21] The vaccination has the potential to significantly reduce the clinical burden of HPV-related disease, the associated high costs of treatment, and the adverse psychological impact which can be caused by the diagnosis of a HPV related disease. [28,29]

Male vaccination not only provides benefits to its recipients but also provides indirect benefits to females and the wider population. This will result in accelerated herd immunity and increase the protection offered to susceptible and high risk groups such as unvaccinated

females, MSM, immunocompromised individuals, and members of the ATSI community.

Furthermore, the introduction of HPV vaccination for all young males and females will further Australia's contribution to the prevention of HPV associated diseases worldwide and provide invaluable data describing the long term effects of HPV vaccination. For a population based primary prevention program to be successful there needs to be strict and persistent surveillance and monitoring of its implementation. Currently, Australia has no national program for the surveillance of HPV or genital warts, although it has setup the NHVPR, which monitors the population vaccination coverage. In collaboration with the PAP test and cancer registries, the information collected through this register should provide invaluable data on the impact of HPV vaccination in females. This monitoring will be extended in 2014 to include males, providing a robust data set enabling the measurement of the impact of HPV vaccination on the incidence of HPV related cancers in the coming years.

Conflict of interest

None declared.

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Mending a broken heart: management options for preventing cardiac sequelae in Kawasaki disease

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Background: Kawasaki disease (KD) is one of the commonest causes of acquired heart disease in children worldwide. [1] Coronary artery abnormalities (CAAs) develop in 15-25% of untreated children with Kawasaki disease. [2] Intravenous immunoglobulins (IVIG) and aspirin have been widely used for the treatment of Kawasaki disease, with proven benefits. Novel drugs may also prove to have beneficial effects in reducing disease progression. [1,3,4] **Objective:** This descriptive review was conducted in order to investigate the efficacy of current and emerging treatment options in preventing disease progression in Kawasaki disease in children. **Methods:** The electronic databases PubMed, MEDLINE via Ovid, Science Direct and The Cochrane Library were reviewed. English language publications from the last 25 years were included. The primary outcome of efficacy was the reduction of CAAs and rate of improvement in febrile illness in children. **Results:** A total of 30 articles were identified. IVIG in conjunction with aspirin were the most useful in reducing the incidence of CAAs. Use of IVIG versus placebo showed a significant decrease in the incidence of CAAs after IVIG at thirty days. [5] Corticosteroids were found to be effective for refractory KD treatment. Etanercept did not appear to worsen the likelihood of CAAs. **Conclusion:** There is strong evidence for the use of IVIG. Combination of IVIG with aspirin was more effective in reducing the incidence of CAAs compared to IVIG alone. Emerging medications such as etanercept, infliximab and ulinastatin seem effective; however, trials are limited and underpowered.

Introduction

Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, is a systemic vasculitis which presents mainly as a self-limiting acute illness of infants and children under the age of five years. It has also become an important disease to exclude upon the presentation of a febrile child. [1,2,6] Worldwide it is one of the commonest causes of acquired heart disease in children. [1,2] While KD has high prevalence in Asians, cases are also being increasingly reported in other racial groups. [1,3] In Asian countries the incidence has increased from 69 to 218 cases per 100,000, in children less than five years of age. This incidence is 10-15 times greater than in the Caucasian population. [2,7] Results of a national scheme conducted in 1994 in Australia revealed the annual incidence of KD was 3.7/100 000 children < five years old. [8]

KD particularly affects the small and medium sized elastic arteries, causing a multisystem inflammatory vasculitis that has a specific tendency to cause coronary artery abnormalities (CAAs) in 15-25% of untreated patients. [1,7,9]. These CAAs can either be coronary artery aneurysms, which are focal dilations of a vessel, or coronary artery ectasia, which is diffuse dilation of the coronary artery. Children presenting with KD are diagnosed mainly by clinical criteria. These have been summarised by the American Heart Association in early 1993 and outlined in Table 1. [1]

Laboratory investigations provide minimal diagnostic utility, but may be useful in excluding other causes of febrile illness in children. [1]

The cause of the development of KD is largely unknown. [4] It is thought that an undefined infectious trigger in a genetically predisposed individual results in the disease. [7] This has been supported by observations of a seasonal peak in disease incidence in the winter and spring months, epidemics with a clear epicentre, and a peak incidence in the toddler age group compared to children who are less than three months old and to adults. [4] A provisional hypothesis is that a bacterial toxin, acting as a super antigen, in turn acting as a trigger; this is based on the existing clinical similarities between KD and staphylococcal or streptococcal toxin mediated illnesses, specifically desquamation and strawberry tongue. [3,4,11] Drug treatments target specific steps of a disease pathway in order to prevent progression of disease. [3] Cytokines such as tumour necrosis factor-alpha (TNF-α), interleukin 1 (IL-1) and interleukin 6 (IL-6) have been noted to increase during the acute phase of Kawasaki disease. [3] It has also been noted that there are higher TNF-α levels in KD patients with coronary involvement than in patients without coronary involvement. [12] Targeting different aspects of disease progression allows the development of new therapeutic interventions. Such developments will be discussed later. [7]

Timely diagnosis and treatment of KD is vital in order to reduce

Table 1. *Criteria for the diagnosis of Kawasaki Disease. [10]*

Criterion	Description
Fever	
Duration of five or more days plus four of the following:	
Conjunctivitis	Bilateral, bulbar, non-suppurative
Lymphadenopathy	Cervical, >1.5cm
Changes to lips or oral mucosa	Red cracked lips, strawberry tongue, or diffuse erythema of the oropharynx
Rash	Polymorphous, no vesicles or crusts
Changes of extremities	Initial stage: erythema and oedema of palms and soles. Convalescent stage: peeling of skin from fingertips
KD may be diagnosed with fewer than four features if coronary artery aneurysms are detected. [1,4,6]	

potentially dangerous or debilitating cardiac sequelae. Cardiac complications of treatment delay and treatment failure include development of coronary artery aneurysms or ectasia in approximately 15-25% of affected children. Other complications that may follow are myocardial infarction or thrombosis. Treatment with intravenous immunoglobulin (IVIG) in the acute phase of Kawasaki disease reduces the risk to 5%. [1,3,4] Early detection and timely treatment therefore has a huge impact on disease progression and treatment of refractory KD. [3,6]

Methodology

A number of databases including Google Scholar, PubMed, Science Direct and The Cochrane Library were searched for papers regarding the treatment options for KD, and from these key terms were identified. The following search terms were used either alone or in combination: Kawasaki disease, Kawasaki disease treatment, Kawasaki disease diagnosis, management of Kawasaki disease, treatments, IL-1, TNF-alpha, pharmacological treatment of Kawasaki disease.

Studies were chosen based on relevance to the literature review focus: the treatment options available for KD, cardiac sequalae, particularly, coronary artery abnormalities. Articles included were published in the last 25 years in the English language. A total of 30 articles were found to be relevant.

Current guidelines for treatment of Kawasaki Disease

There are a number of different guidelines worldwide for the treatment of KD, but there is general consensus that prompt treatment of KD significantly reduces disease progression (Table 2). [1]

As seen in Table 2, the use of aspirin and 2.0 g/kg/per day of IVIG is the recommended treatment for KD. IVIG is given as early as possible with variation in the dosages of aspirin required, especially in the acute phase of the disease.

Table 2. *Comparisons of guidelines for treatment of Kawasaki disease.*

Country Guidelines	IVIG	Aspirin
Australian Royal Children's Hospital Melbourne	Immediate hospital management and commencement of 2 grams/kg of IVIG over 10 hours within 10 days of illness. [13]	3-5 mg/kg of aspirin given once a day for 6-8 weeks. [13] An echocardiogram done at initial presentation and, if negative, again at 6-8 weeks. [13]
American Heart Organisation	Single dose of 2 g/kg IVIG. [1]	High dose aspirin of 80-100 mg/kg divided into four doses. [1]
United Kingdom (National Institute of Health and Excellence)	IVIG 2 g/kg as a single infusion over 12 hours.	30-50 mg/kg/day of aspirin divided into four doses. [14] Ongoing aspirin 2-5 mg/kg/day when fever settles, minimal duration of 6 weeks depending on echocardiogram and ECG investigations.

Treatment options for Kawasaki Disease

Salicylate

The acute phase of KD causes marked inflammation and, as a result, there is a conformational change in coronary artery endothelium. [3,4,13,14] Aspirin is widely used for a number of medical conditions, and its anti-inflammatory effects are of great benefit to those diagnosed with KD. [3] Aspirin has anti-inflammatory, antipyretic and antiplatelet effects, which make it ideal in this acute phase and for long term management of the disease. [1,6,14] In low doses, aspirin inhibits platelet generation of thromboxane A2, resulting in an antithrombotic effect. The main concern with long term use of aspirin in children is the risk of toxicity. [6,15]

It has been shown that there is no difference in the incidence of CAAs in patients who are treated with high dose (> 80 mg/kg/dose) versus a low dose (< 80 mg/kg/day) of aspirin in the acute phase of KD. [14] In North America, use of high doses is accepted during the initial phase, while in Japan, concern about toxicity has led to moderate use (30-50 mg/kg/day) in the acute phase. [1]

A Cochrane review analysed randomised controlled trials of the use of salicylate in treatment of KD. Only one relevant study was identified, which compared aspirin alone to aspirin plus IVIG. [6] There was no difference in the incidence of CAAs up to 30 days following disease onset between patients treated with IVIG 200 mg/kg daily for five days and patients treated with IVIG 200 mg/kg plus 35-50 mg/kg/day of aspirin. [6] The data collection period was limited to 60 days, therefore the study was unable to identify any deleterious effects of either regime over a longer period. [6] The use of aspirin did not appear to add a benefit when used with IVIG, but not using aspirin altogether was not effective in reducing CAAs. There is a lack of randomised controlled trials focusing on this issue, and currently there is not enough evidence to recommend the omission of aspirin in treatment of children with KD.

There is also evidence that in the acute phase of KD there is reduced absorption and increased clearance of aspirin. When higher doses are used, therapeutic levels are usually not reached. [16,17] However, hepatotoxicity, gastritis and gastrointestinal bleeding are common concerns with using high dose and long term aspirin regimens, with the possibility of developing Reye's syndrome in the children treated. [13-15,17] Although adverse effects from the use of aspirin were not identified in randomised controlled trials, this lack of evidence could be attributed to the short duration of follow-up in these trials.

Intravenous immunoglobulins (IVIG)

Studies from Japan have shown that administration of IVIG during the initial acute episode of KD has a considerable impact on reducing coronary artery abnormalities. [5,18] IVIG is a blood-based product which contains pooled, polyvalent IgG extracted from the plasma of human donors. [18] It has generalised anti-inflammatory effects which help reduce fever and the acute markers of inflammation associated with KD. It is understood that once IVIG is injected, it forms an immune complex which interacts with Fc receptors on dendritic cells and as a result mediates anti-inflammatory effects. [7,19] This in turn reduces the severity of the inflammatory state and reduces the conformational changes of the coronary arteries, therefore reducing coronary ectasia; however, the complete mechanism of action is unknown. [5,20,21]

A meta-analysis of existing randomised controlled trials compared the effectiveness of IVIG with a number of different interventions. [5] Results showed that IVIG was significantly better than placebo in reducing new CAAs, at 30 days (RR = 0.74, 95% CI 0.61-0.90).[5] There was no difference between the groups at 60 days. The meta-analysis showed that when 400 mg/kg/day of IVIG was used for five days versus 2 gm/kg in a single dose there was a reduction in CAAs at thirty days after using the higher single dose (RR = 4.47, 95% CI 1.55 - 12.86). [5] There was also a significant reduction in duration of fever with the higher doses. [5] IVIG did not seem to be associated with an increase in adverse events, although IVIG can have important adverse effects, including headache, dermatitis, pulmonary oedema, anaphylactic reaction, acute renal failure, venous thrombosis and aseptic meningitis. [5,14]

Overall, it was found that using higher doses of IVIG per kg was more beneficial than using lower doses. There was no difference between different types of preparations of IVIG and the incidence of adverse effects. [1,5] Randomised controlled trials and meta-analyses have

confirmed that IVIG plus aspirin is more helpful in reducing risk of CAAs compared to aspirin alone. [1,5,6] Although aspirin does not appear to effect aneurysm formation, all trials of IVIG treatments have included the use of aspirin with IVIG, as it was the treatment of choice prior to IVIG development. Further, as there is insufficient evidence about the use of IVIG alone, use of aspirin in conjunction with IVIG continues. [6]

Corticosteroids

Interest in the use of corticosteroids developed when children continued to develop CAAs despite effective IVIG and aspirin treatment. [1,14,22] Glucocorticoids have a number of mechanisms of action. The most important for the treatment of KD are the potent anti-inflammatory effects. [23]

A multicentre, randomised, double blind, placebo-controlled trial in 2007 determined the effect of adding methylprednisolone to conventional primary therapy in reducing CAAs. [19] All patients received the conventional therapy of IVIG of 2 g/kg and aspirin 80-100 mg/kg per day until children were afebrile for 48 hours, then 3-5 mg/kg per day of aspirin from that day on. Methylprednisolone 30 mg/kg was given as a single intravenous dose to half of the participants. It did not improve coronary artery outcomes at week one or five. [1,19] Its use shortened the duration of the initial period of hospitalisation and accelerated the recovery of laboratory biomarkers such as estimated sedimentation rate (ESR) at week 1 ($p = 0.02$) and tendency for lower c-reactive protein (CRP) ($p = 0.07$). [19] The total number of days of fever and of hospitalisation did not differ between the intervention and control group. [19,24-26]

Children who had a persistent fever and who then received retreatment with IVIG and IV methylprednisolone showed improved that coronary outcomes when compared to the placebo group, indicating that children with higher risk for CAAs may benefit from glucocorticoid treatment. [19] Limitations of this study included that only a single dose of IV methylprednisolone was used as the intervention, and the study focused on a relatively low risk population. There are limited data available on possible adverse effects from its use due to short duration of follow-up. [19]

Similarly, a Cochrane review focusing on steroid use in KD found that steroids did not reduce the incidence of coronary artery aneurysm. Several of the studies identified were limited by the quality of the study design and by sample size. [3,25,27] A meta-analysis published in 2012 showed a significant reduction in the rates of initial treatment failure among those who received corticosteroid therapy in combination with IVIG compared to IVIG alone (Odds Ratio: 0.05; 95% CI: 0.32-0.79; $p = 0.003$). [25] This supported the study by Newburger and colleagues (2007), which showed that the use of corticosteroids reduced the time required for CRP to return to normal. Although corticosteroid therapy combined with IVIG in primary treatment or as treatment for IVIG-resistant patients improved the clinical course without increasing coronary artery abnormalities in children with acute KD, it did not cause any reduction of already existing CAAs. [25]

Future treatments and research

According to current American Heart Association guidelines, further IVIG is required to reduce cardiac sequelae if patients have a recurrent fever beyond 36 hours after completion of the IVIG infusion. [1] This highlights the importance of developing further treatments to prevent treatment failure.

As previously mentioned, serum levels of inflammatory cytokines such as TNF-α, IL-1 and IL-6 are increased during acute KD. [3,4] A higher percentage of patients with coronary artery involvement were also TNF-α positive. It is postulated that TNF-α activity plays an important role in the pathogenesis of Kawasaki disease. [3,4,28] This cytokine promotes conformational changes to the arterial endothelium and offers a potential mechanism for development of vascular diffuse dilatation and coronary artery aneurysms. TNF-α inhibitors fall into two classes, monoclonal antibodies and soluble receptors. [1,3] Both etanercept and infliximab (a monoclonal antibody against TNF-α) have beneficial effects on the treatment of KD. [12,28]

A prospective open-label trial of etanercept in patients with KD in conjunction with IVIG and aspirin was inconclusive in determining the benefit of adding etanercept to IVIG. [12] Patients received a 0.8 mg/kg/dose of etanercept immediately after IVIG infusion, and then received a weekly dose. [12] Fifteen patients completed the study, and they did not require retreatment with IVIG for persistent or recurrent fever, nor did they have worsening coronary artery involvement/cardiac dysfunction. [12] This study was underpowered due to the small sample size and therefore could not determine if adding etanercept to IVIG and aspirin was beneficial. A randomised controlled trial of this combination would be effective for both acute phase and refractory phases of the disease.

Similarly, infliximab controls disease progression and improves outcomes in IVIG-resistant KD. [29] A retrospective chart review in 2007 compared the duration of fever and coronary artery dimensions of patients with KD. [29] Patients who had their first retreatment with infliximab defervesced earlier and had a shorter hospital stay than those retreated with IVIG. However, coronary artery outcomes and adverse events were similar in both groups. [29] This was a retrospective chart review in one hospital, so the general applicability of the results is limited. Further large scale randomised studies are needed to guide practice.

In a retrospective study published in 2011, 369 patients were treated with a combination of Ulinastatin, aspirin and IVIG for initial therapy in the acute phase, compared to 1179 patients treated with conventional initial treatment of IVIG and aspirin. [30] Ulinastatin reduces neutrophil counts, and causes high plasma levels of neutrophil elastase, improving IVIG's effectiveness, and as a result reduces the occurrence of CAAs. [30] CAAs were reduced in the group receiving Ulinastatin in comparison to the control group; 3% versus 7%, respectively ($p = 0.01$). [30] Many of the CAAs occurred in patients who had refractory KD, but the occurrence of CAAs was less likely in the Ulinastatin group compared to the control group; 13% versus 22%, respectively ($p = 0.001$). [30] Due to the retrospective nature of this study, despite being adequately powered, more evidence is required before changing practice.

Conclusion

It is important to exclude Kawasaki disease in the commonly presenting febrile child. It is the leading cause of acquired heart disease in children under the age of five. Coronary artery abnormalities are an important complication of a failure of KD treatment, affecting 15-25% of untreated children. Timely diagnosis and treatment with high dose IVIG and aspirin is supported with the best level of evidence and appears to be the most effective way of treating KD. In patients with recurrent KD, or failure of the initial therapy, use of adjunctive treatments such as corticosteroids, TNF-α inhibitors and Ulinastatin have some benefit. However, large scale randomised controlled trials are required to support future evidence based practices.

Conflict of interest

None declared.

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Reaping the benefits of collaboration in medical research – Two case histories

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Collaboration is the buzzword in medical research. The prevailing wisdom is that science is now so complicated and expensive that it requires the combined efforts of several individuals and often institutions to solve the problems confronting us. Rarely do we see an original article published in a scientific medical journal with a single author and many articles have more than five authors. Even allowing for the persisting tradition of the head of the research group or the laboratory where the research took place assuming the position of the last (synonymous with senior) author even if their input was minimal, the proliferation of authors does attest to the need to bring multiple minds and skills together to solve problems. This is also reflected in the frequency with which the Nobel Prize for Physiology or Medicine is awarded to two or three scientists rather than to one.

What does collaboration mean and is it always good? Perhaps a clue comes from the definition in the Australian Concise Oxford Dictionary. As well as the obvious and virtuous definition of "collaborate" as "work jointly" there is also the second use as "cooperate traitorously with an enemy". Although we would not envisage the second definition applying in any sense to the most noble and idealistic world of medical research, the alternative definition does warn us that collaboration must be established with the finest motives and with sufficient planning if its benefits are to be realised.

The concept of collaboration is not new of course. Ever since men and women came out of their caves and started to live together in communities they discovered that their communities prospered if individuals were prepared to work together even if it meant that the immediate short-term interests of individuals had to become secondary to the long-term interests of the whole community. More can be achieved if people work together. Although we might think of this as an altruistic activity it is in fact a pragmatic one as evidenced by competing private organisations forming collaborative arrangements to their mutual benefit. Code sharing and shared loyalty programs between competing global airlines are obvious examples.

What examples are there of collaboration in medical research which are not good and where benefits are not realised? The most obvious is where a collaborative grouping is formed in order to apply jointly for research funding from government or commercial sources but there has not been a true coming together of minds and motives. In this situation, if the funding is obtained, there is often a cynical division of the available funds between the "collaborating" parties and the research goes on without the true benefits of collaboration. Alternatively, the application may be made in good faith, the collaboration initiated and then a breakdown of the relationship may occur with the collaboration collapsing. Medical researchers are driven, intelligent but often somewhat egotistical individuals and sometimes there is not enough room in a single collaboration for more than one ego! This is not too different from a number of other areas where high achieving individuals are required to work together. Collaboration does not require the partners to be the best of friends (although that helps). However, it does require a genuine contribution to the collaboration, which may mean less personal glory, and subverting passionately held views of what needs to be done to the decision of the collaborative group as a whole.

Professor Richard Larkins. Source: www.monash.edu.au

I would like to illustrate large-scale collaboration in medical research by two initiatives I am privileged to be associated with.

The first is EMBL Australia. The European Molecular Biology Laboratory (EMBL) is an initiative of 20 European countries which each pay an annual subscription to support medical research and research training headquartered in a large research institute and training centre in Heidelberg, Germany. There are so-called outstations in Monterotondo (Rome) dedicated to mouse genomics and physiology, Hamburg and Grenoble each with synchrotrons and dedicated to structural biology and in Hinxton (Cambridge) dedicated to bioinformatics (the European Bioinformatics Institute, EBI). Australia is obviously not part of Europe, but Australia has been admitted as the first Associate Member of EMBL. This provides access to the magnificent and expensive scientific equipment at EMBL and opportunities for Australian PhD students and postdoctoral students to compete for and gain entry to the prestigious student research training positions. It has allowed Australia to establish EMBL groups and to form the Bioinformatics Resource Australia EMBL at the University of Queensland. The Australian partners that form EMBL Australia are Monash University, the Universities of Queensland, Sydney, Western Australia, Melbourne, Adelaide, NSW, the Australian National University and CSIRO. Two outstanding young group leaders have been appointed for the partner laboratory at Monash University headed by the Scientific Head of EMBL Australia, Professor Nadia Rosenthal, formerly Head of EMBL in Monterotondo. Furthermore, a PhD School is starting in 2013, where PhD students are being sent to seminars in Heidelberg. A group leader currently at EMBL in Heidelberg will return to the University of Sydney in 2015. Three group leader positions are being established at the new South Australian Health and Medical Research Institute which is affiliated with the three universities in South Australia. The Bioinformatics Resource at the University of Queensland is being developed under the leadership of Graham Cameron, previously Associate Director of the EBI and will be a major repository of genomic and proteomic data and a link with the EBI.

EMBL Australia is extending to Australia a great example of scientific collaboration established in Europe. EMBL is now the highest ranking

medical research institute outside the United States in terms of quality and impact of its scientific publications and ranks alongside the best US institutes. It is producing the leaders of medical science for all of Europe and indeed many alumni lead science in countries outside Europe. EMBL Australia is building collaborative links with Europe as well as fostering collaboration in research, data management and analysis and research training amongst the leading research universities in Australia and CSIRO.

As in every collaboration, it takes considerable work to maintain effective partnership and not to lose sight of the main game because of petty squabbling. At the European level, the financial crisis in Europe makes Council meetings fraught with arguments about the extent of the budget and the individual financial contributions. At the level of EMBL Australia, benefits come to the various contributing partners at different times and those partners yet to receive benefits ask what is in it for them. This is natural, but the big picture has to be kept constantly in mind. If each partner thinks only of benefits that might accrue to them, the collaboration will fall in a heap.

The second collaborative initiative I would like to describe is the Victorian Comprehensive Cancer Centre (VCCC) in Melbourne. The Victorian and Commonwealth governments have each contributed over $425m to establishing a new billion dollar plus building on the site of the old Melbourne Dental Hospital. It will house the relocated Peter MacCallum Cancer Centre, new cancer research laboratories for the University of Melbourne and be connected by aerial walkways to three new floors for cancer services in the Royal Melbourne Hospital which shares the precinct with other partners in the VCCC, the Royal Women's Hospital and the Walter and Eliza Hall Institute. Other members of the VCCC which are not collocated are the Royal Children's Hospital, the Western Hospital and St Vincent's Hospital.

The concept and definition of a "comprehensive cancer centre" comes from the National Cancer Institute (NCI) in the USA. The NCI uses the term to indicate an institution which offers state-of-the-art care and services that include a strong research base along with a variety of prevention, care and educational activities that serve the community. None of the current partners do all these things and the aim of the joint venture is to create a collaborative centre which not only delivers the highest quality care but also world leading research, cancer prevention and community and professional education of the highest standing. To achieve all these benefits, each of the partner institutions has to sacrifice some of their autonomy in the interests of the collaboration. This places each of the CEOs of the partner institutions in a difficult situation at times. There often appears to be a conflict between what seems best for their institution and their employees compared with decisions which are required to achieve all the potential that the VCCC offers. Such is the nature of collaboration.

A census and analysis of the citation data arising from the research publications of the partners in the VCCC indicates the power of collaboration in enabling good science. An analysis of the "impact factor" of cancer publications commissioned by the VCCC Executive Director Professor Jim Bishop and conducted by Linda Butler, showed that Australian cancer publications outperformed the world average, publications from Victoria outperformed those from the rest of Australia, while those from the VCCC partners outperformed those from the rest of Victoria and those from VCCC partners with collaboration between VCCC partners or between VCCC partners and external partners outperformed publications without such collaboration.

As medical research becomes more and more expensive and complicated, collaboration will become more and more necessary. It will not necessarily become any easier, but we must all work together to overcome the barriers. Young researchers with their flexible and idealistic but practical approach are in the best position to facilitate this.

The Federal Budget 2013 - 2014: An opportunity to deliver a health workforce that meets future healthcare needs

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Associate Professor Leslie E. Bolitho AM is a consultant physician in internal medicine and has been practicing in Wangaratta, northeast Victoria, since receiving his FRACP in 1983. He is currently President of The Royal Australasian College of Physicians (RACP). Associate Professor Bolitho has been involved with the RACP as Council member (2001-2003) and then Board Director (2005-2008). He was elected as a member of the Adult Medicine Division Council 2005-2010 and has also served on various State Health department committees. From 2001 to 2003, Associate Professor Bolitho held the position of President of the Internal Medicine Society of Australia and New Zealand (IMSANZ). From 2005 to 2009 he was President of the Australian Association of Consultant Physicians (AACP), an advocacy body representing consultant physicians.
Associate Professor Bolitho AM was appointed as a Member of the Order of Australia in 2010 for services as a clinician and educator and for his work in the development of rural and regional health services in northeast Victoria. In 2005 Associate Professor Bolitho received the RACP Medal for Outstanding Service to Rural and Remote Areas, and in 2008 was presented with the Victorian Rural Doctors Award for Outstanding Contribution to Rural Communities (RWAV).

The Federal Budget 2013 – 2014 announcement and its expected impact on health

The announcement of the Australian Federal Budget is one of the most important dates on the calendar for the healthcare industry. The Budget provides a clearer understanding of the funding priorities of the Federal Government and lays the foundation for healthcare investment. This upcoming Federal Budget, to be announced on 14 May 2013, comes at a crucial time, with pressure on the Federal Government to deliver a tight fiscal Budget, advance the National Disability Insurance Scheme (NDIS) and carefully navigate through issues of state and territory jurisdiction. Issues relating to medical graduates are particularly poignant, with protected teaching, health workforce capacity, and the provision of general medicine in the rural and remote setting critical areas that must be addressed in the upcoming Federal Budget. The challenges all medical colleges currently face relate to the provision of training that prepares trainees for the challenges ahead, the adoption of technology into education models, and the applicability of training across remote, regional and metropolitan communities and settings outside of the hospital.

The current state of the Australian health system

The health of Australia's population is ranked among the best in the world. However, increasing life expectancy brings with it the challenges of an ageing population, particularly to a healthcare system that is designed for, and accustomed to, episodic acute and emergency care, and single disease presentations. Patient interactions with the healthcare system are now more regular and complex and healthcare professionals are commonly involved in delivering care across a range of settings, including acute and sub-acute hospitals on an inpatient or outpatient basis, the home, primary care clinics and aged care settings. Healthcare expenditure is ballooning and additional demands are being placed on an already strained health workforce. [1]

Jurisdictional funding and policy responsibilities and the public-private divide have resulted in a fragmented and siloed healthcare system. As a result, patients experience difficulty navigating through the system and specialist physicians confront challenges trying to integrate and coordinate with other members of the multidisciplinary team. There are opportunities to overcome these barriers to improve the healthcare system and health outcomes for all Australians, particularly in the context of National Health Reforms. Areas highlighted by the College as most impacting for medical graduates and physician trainees include the equitable distribution of the physician and trainee workforce, protected teaching, and issues of health workforce, specifically general medicine.

One of the greatest strengths of the Australian healthcare system is the increased numbers of medical students who will eventually undertake specialist physician training. Recognising that there are challenges associated with increased numbers, the RACP and other medical colleges will need to work with the Federal Government to ensure all medical graduates receive their desired and best possible experiences in the various training programs. Increased numbers of trainees will eventually equate to increased specialist physicians and other healthcare professionals. It will be important to ensure these numbers are mobilised effectively and are trained to operate in a number of different healthcare settings.

Protected teaching

There is a need for protected time for supervisors for training and education. In addition to the increased numbers of medical graduates entering physician training, improvements to the structure of the training programs in accordance with standards set by the regulators (the Medical Board of Australia and the Australian Medical Council) means that there is a need to increase the length of time for supervisors to support trainees in their learning. This has been identified as a key priority area by the RACP and many other Australian medical colleges ahead of the Federal Budget funding allocation in May 2013.

The RACP recommends the Australian Government work with the RACP, other medical colleges and jurisdictions to increase the capacity of specialist physicians to train the future physician workforce. Increased capacity could be achieved by facilitating the introduction of protected time for supervisors and trainees to undertake training activities, and facilitating an increase in the time needed for supervisors to be available to support trainees in their learning in the workplace. This includes attending supervisor training and professional development as well as allocated time to meet with trainees to review progress, provide advice and complete supervisor reports. A further key action

is the facilitation of better training for supervisors, recognising that the supervisor role requires specific knowledge and skills.

Ensuring the equitable distribution of the physician and trainee physician workforce

The health workforce must consist of sufficient numbers and skill mix, and services must be fairly distributed across populations to manage the current and future healthcare needs of the Australian population. The specialist physician workforce must have capacity to train new specialist physicians and take the time to develop and improve knowledge and skills for the provision of high quality and safe clinical care.

People living in regional, rural and remote areas have some of the highest rates of complex and chronic disease. However, these populations have the poorest access to locally provided specialist healthcare. There is a need for specialist services to be distributed fairly across populations and located where they are needed the most. Vulnerable communities, particularly those that experience higher rates of long term illness, must be able to access specialist services without difficulty.

The RACP is seeking to work with the Australian Government to continue to support the redistribution of specialist physician services toward rural and non-hospital settings through Specialist Training Program (STP) placements. The RACP recommends the continuation of STP funding towards rural training places, rural salaries and 'Rural Support Loading' to supplement the additional costs incurred by trainees in rural areas. Additional measures put forward to the Government as part of Federal Budget priorities include the continuation of STP funding towards training places in community, non-clinical and ambulatory care settings and the continuation of STP funding towards posts in Aboriginal Controlled Community Health Services and Aboriginal Medical Services. Specialist training is heavily reliant on the skills and availability of clinician teachers and supervisors in the workplace. The STP provides a Commonwealth-funded annual salary contribution of $100,000 until 2015 for trainees in non-traditional settings.

In an integrated national healthcare system, healthcare practitioners would be able to provide timely and quality care in the setting that best meets patient needs, as summarised by the phrase "the right care, at the right time, by the right provider, in the right setting." The current debate about future workforce shortages as well as the distribution of specialist physicians, which is often mismatched with patient needs, reinforces the importance of care delivered in all settings.

Indicators of a high-quality and highly functioning health system include the capacity to provide timely and safe care to patients in the setting that best meets their needs and preferences, and the ability to mobilise multidisciplinary teams to provide care in an integrated and coordinated manner.

The RACP strongly supports measures that equip medical graduates with the skills to manage the increasing prevalence of comorbid chronic disease in the community. This includes developing training pathways that enable more generalist and dual trained physician workforce that can respond to this shift in demand, as well as targeted distribution of the physician workforce, particularly to better meet the needs of rural and remote communities. This is particularly relevant for today's medical graduates, who will play a significant role in shaping the future state of Australia's healthcare landscape.

There is growing evidence to support the adoption of collaborative organisational arrangements for the provision of care in the Australian healthcare system. The development of formal arrangements that allow specialist physicians to regularly provide care to Aboriginal and Torres Strait Islander communities and older people in primary and aged care services to address unmet demand is imperative. To counter this unmet demand, the RACP recommends careful consideration and analysis of specialist medical services that could be delivered in primary, community and ambulatory settings. The Australian Government must invest in cost-effective interventions tailored to redesign service delivery and widely promote a multidisciplinary team-based approach for the provision of chronic and acute care in the primary, community and ambulatory settings.

As the physicians of the future, trainees and medical graduates play a vital part in the development of a cost-effective, equitable and high-functioning healthcare system. Working collaboratively to develop models of healthcare that benefit and respond to all communities, age groups, and unique circumstances is key to addressing the complex challenges facing today's healthcare landscape.

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The making of a surgeon

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Michael is a General Surgeon at Westmead Hospital, and Clinical Associate Professor of Surgery at Western Clinical School of Sydney University. He has post-graduate training in gastro-oesophageal and hepatopancreatobiliary surgery. Michael trained at St Vincent's Hospital in Sydney and later at The Royal Postgraduate Medical School and Guys Hospital in London. He then worked in Beth Israel Hospital and Harvard Medical School, Boston and Queen Mary's Hospital, Hong Kong before joining Westmead in 1986. He has Fellowships of The Royal Australasian College of Surgeons, Royal College of Surgeons of England and American College of Surgeons and was elected to Council of RACS in 2006, was Treasurer 2010-2011 and elected President in 2012.

Surgery is a therapeutic response to a sometimes critical need for technical intervention. In ancient times, there were tried and sometimes true procedures – nothing else was known. The barbers had basic instruments and could be awfully quick. Early references to surgery talk of fixing fractures, trephining the skull or the removal of arrows. Thus, early surgeons were dependant on experience and technical expertise. A detailed medical knowledge was not required. As surgery the profession developed, surgical training was apprenticeship-based, with no structured curriculum and trainees were not encouraged towards individual thought. What the chief surgeon did, they repeated without question.

During the first part of the 20th Century, people actually survived appendicectomy and gangrenous war wounds. In 1930, the simple nasogastric tube transformed the management of bowel obstruction. After World War II there was an explosion of scientific advances profiting both the profession and society. Safer anaesthesia, antibiotics, an understanding of fluid and electrolyte balance all made surgery safer. The boundaries of operations were expanded. Aged and less fit patients became candidates for surgery. In parallel the costs of medical care rose exponentially and government increasingly assumed a greater responsibility for the costs, as well as regulation of the providers of healthcare. Patients have become more assertive about the quality and provision of healthcare provided, within their own societies. These historical forces have shaped the profession surgical trainees choose to enter.

Surgery is no longer just the practice of technical expertise on a background of medical knowledge. Surgeons are not barbers armed with 21st Century knowledge. The surgeon's non-technical skills are now rated equally with his or her technical ones. Surgeons must be able to communicate, collaborate, be sensible with their own lives, demonstrate leadership, assume managerial roles when required and teach the next generation(s) – all wrapped in a calm professional exterior.

In Australia and New Zealand, potential surgeons enter training within the programs of Specialist Surgical Societies , in partnership with the Royal Australasian College of Surgeons, proceeding on to a Fellowship of the College after an exit examination. Selection to surgical training in Australia and New Zealand is based on a national selection process undertaken once a year. Applicants are assessed

Table 1: Specialist Surgical Societies

Cardiothoracic Surgery
General Surgery
Neurosurgery
Otolaryngology Head and Neck Surgery
Orthopaedic Surgery
Paediatric Surgery
Plastic and Reconstructive Surgery
Urological Surgery
Vascular Surgery

Associate Professor Michael Hollands.

on the basis of curriculum vitae, referees' reports and an interview. Training is conducted in one of nine surgical specialities (Table 1). Applicants may apply to more than one surgical specialty. Application for a position in the SET Program may be made as early as the second postgraduate year (PGY2) and training can start in PGY 3. There are certain eligibility criteria – which vary between the specialities - and these are available on the College website (http://www.surgeons.org). Because it is a national selection process, a requirement of the ACCC

Table 2: 9 Surgical Competencies

Professionalism
Teacher and Scholar
Health Advocate
Manager and Leader
Collaborator
Communicator
Medical Expertise
Judgement – Clinical Decision Maker
Technical Expertise

and AMC, trainees from Victoria, may for example, be appointed to a training position in Western Australia. Applicants considering more than one specialty must apply to each speciality.

Successful applicants commence the Surgical Education and Training program (SET). Education implies acquisition of knowledge and via training the acquisition of skills. The SET Program aims to train surgeons based on the nine competencies outlined by the Royal Australasian College of Surgeons (Table 2). Medical knowledge and technical expertise are only two of the nine competencies.

The SET Program aims to produce surgeons of a competent standard, capable of independent practice and of functioning with other health professionals, within a multi-disciplinary clinical team.

The duration of training is dependent on achieving competence and is usually five years. Trainees are allocated to accredited training positions by the specialist society responsible for their training. They will complete a number of placements or rotations across a number of areas of clinical practice. They are assessed on their performance by the consultants for whom they work, overseen by the designated supervisor of surgical training. Trainees will also be rotated to a variety of hospitals giving them exposure to urban referral hospitals, major suburban hospitals and regional/rural hospitals. Progression through training is seamless providing clinical progress occurs across the nine competencies. Typical progress has been mapped by College research, noting variation in individual competency levels due to individual and rotational differences. In brief, experience cannot be standardised.

Successful completion of training is not determined solely by satisfactory clinical performance. Training is assessed in an objective fashion also. Within the first year of training trainees must complete a generic and a specialty specific science examination, as well as a generic clinical (OSCE-style) examination. This ensures all trainees have a core of scientific knowledge applicable to the clinical practice of surgery. Increasingly trainees seek additional training in anatomy and a variety of opportunities are available for this. In some Australian States anatomy courses are provided for junior doctors, who may in turn practise a variety of medical disciplines apart from surgery.

Trainees are expected to complete a number of courses during their training. These may include ASSET (Australian and New Zealand Surgical Skills Education and Training), CCrISP (Care of the Critically Ill Surgical Patient), EMST (Early Management Severe Trauma) and CLEAR (Critical Literature Evaluation and Research). Details about these courses are available on the College website.

Objective clinical assessment is on-going throughout training. Assessment includes review of logbooks and mid- and end of - rotation assessments. Clinical assessment is based on DOPS (Direct Observation of Clinical Skills), Procedure based assessment (PBS) and directed clinical examination scenarios (mini-CEX). These assessments are used to inform the individual rotation consultants and supervisors of surgical training how the trainee is progressing. Progress is discussed with the trainee both at mid- and end of- term. Such discussions facilitate goal setting in general, as well as to identify any areas for remediation

All the training programs also predicate a research component. The requirements vary with the different programs but generally require the trainee to present a paper at a significant clinical meeting, and in some societies to have a paper accepted for publication. Although sometimes perceived as a further hurdle preparing a piece of research entails collecting and analysing data, reviewing the associated literature critically and collating ones thoughts logically.

As the completion of training approaches the supervisor of training approves the trainee to sit the Final Fellowship Examination. Approval is based on attaining clinical competence, which includes satisfying all 9 competencies and research requirements. The Final Examination aims at documenting a competent surgeon in his or her chosen speciality. There are several modules which particularly evaluate medical knowledge, judgement and clinical decision making, as well as communication and professionalism. Technical skills, collaboration, the scholar and teacher, health advocacy, leadership and management are continually assessed through the SET program. These assessments depend significantly on the surgical supervisors.

It is important that trainees take some ownership of their training. Identify what YOU need to know and where to find it. Set goals, engage YOUR surgeons (the trainers!) and use the assessment tools. Goal setting can be characterised by the acronym SMART: specific, measureable, attainable, relevant and time-bound. Setting goals, especially at the start of a six-month rotation, begins the dialogue about one's needs and thus future progress.

At the completion of surgical training surgeons should be able to practice independently: competently and safely. The new surgeon cannot expect to be proficient as an expert in every aspect of their field. Many will seek further training in an area of special expertise. For example a general surgeon may sub-specialise as a hepatobiliary surgeon, an orthopaedic or neurosurgeon as a spinal surgeon. The College does not undertake or supervise this training but appropriate training programs are organised by surgical societies. Examples include the Spine Society or the Australasian Hepatopancreatobiliary Association. This post-Fellowship training is undertaken as a 'Fellow', something akin to the UK Senior Registrar system.

Opportunities also exist for young surgeons to travel overseas for further training, whether in defined overseas 'Fellowships' or quality service roles, which provide supervised experience. The availability of such training is dependent on the registration requirements of the nation involved. Academic surgery is also a possible career choice and the College provides over $800,000 in scholarships annually to facilitate this. Similarly many surgeons opt to go into rural, regional or outer metropolitan practice.

At the completion of training a surgeon in Australia and New Zealand has a wide range of skills which enable him or her to function competently. Proficiency in the field, or expert practice requires time in the chosen field of practice. Ongoing clinical work, supported by senior colleagues where appropriate, enables the development of that expert proficiency. Completion of (SET) training is just that – it marks the beginning of a professional life, to be continually refined and developed throughout one's years of clinical practice. The College encourages involvement of Fellows in its activities. Hopefully each generation of new surgeons will, in the years to come, continue to participate in the evolving educational programs of the College, and The College facilitates this opportunity through the Academy of Surgical Educators, providing surgeons with skills as educators as well as the skills expected of a surgeon.

Some surgeons, once their training is complete, will achieve proficiency and do good works outside of Australia and New Zealand, be they in less fortunate countries or the prominent centres especially in the Northern Hemisphere. Surgery is global, and political and immigration regulations aside, the RACS expects its diplomates to be noted as ambassadors for the College in particular, and Australia and New Zealand in general.

The doctor-patient relationship and its effect on the health of Indigenous Australians

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There is a significant gap in life expectancy between Indigenous and non-Indigenous Australians. This may be due to a number of factors including demographics and poor accessibility to health care, but also to a lack of trust in, "Western medicine" and poor engagement with services. This report considers the cases of two Indigenous patients who presented to Sydney hospitals, in the context of the doctor-patient relationship. The cases and the relevant literature demonstrate that language and cultural barriers for communication between Indigenous patients and health-care staff are numerous, and that the use of clear language, teaching illustrations, informative CDs and DVDs should be emphasised. The presence of an Indigenous Liaison Officer during hospital consultations can be helpful for both the patient and the staff. A good therapeutic relationship is invaluable in gaining Indigenous patients' trust and improving health-care outcomes. Access and availability of Indigenous Liaison Officers and interpreters is increasing, and the importance of cultural sensitivity and staff training to enhance communication with Indigenous patients is increasingly evident. Continued efforts may move us one step closer to reducing the health-care gap.

"I will remember that there is art to medicine as well as science and that warmth, sympathy and understanding may outweigh the surgeon's knife or chemist's drug."

Hippocratic Oath (1964)

Introduction

In 2011, the Australian Institute for Health and Welfare reported a significant gap in life expectancy between Indigenous and non-Indigenous Australians. This gap was 11.5 years for males and 9.7 years for females. [1] Non-communicable diseases explains 70% of the health gap, with cardiovascular disease as the leading cause group (23%), followed by diabetes (12%), mental disorders (10%) and chronic respiratory disease (9%). [2] Many socio-political factors including low socio-economic status, poor accessibility to health care, history of colonisation and marginalisation have contributed to this health gap but poor engagement in services by Indigenous patients as a contributing cause has received increased attention in the recent years. [3] Lack of trust of, "Western medicine" has been suggested as an important mediating factor in poor engagement and access. [4]

As illustrated by the Hippocratic Oath, an empathetic, trusting doctor-patient relationship has always had the utmost regard in the practice of medicine. The quality of the relationship between the patient and health care practitioner is a predictor of adherence to treatment and outcomes. [4] Likewise, poor engagement between doctors and patients is found to be associated with negative outcomes for both patients and doctors. [5] Patient satisfaction improved and emotional distress among patients reduced with better doctor-patient communication. [6]

This report will portray the cases of two Indigenous patients at Sydney hospitals and discuss some of the barriers that Indigenous patients face. It will also illustrate the importance of a trusting relationship between the medical team and Indigenous patients, and give evidence-based suggestions on how to improve health-care outcomes in this population.

Case 1

Ms. NW, a 39-year-old lady who identifies as Indigenous, was brought in by ambulance after multiple episodes of haemetemesis in the preceding eight hours. She also complained of painless menorrhagia with many clots for the past four weeks. This presentation was on a background of chronic alcohol abuse and liver cirrhosis. Ms. NW was investigated and found to have a normocytic, normochromic anemia (Hb 63g/L), in keeping with her acute blood loss. Her liver function tests were consistent with the history of alcoholism and liver disease (raised GGT and AST), and she was found to be in a coagulopathic state (thrombocytopenia; elevated PT and aPTT; INR=1.8). Ms. NW's management included blood transfusions.

Ms. NW was stabilised and discharged yet her treating team were concerned about her long-term outcome, compliance with treatment and lifestyle modifications, and future health. The discharge plan recommended the involvement of a social worker and an occupational therapist but Ms. NW refused these services saying, "I can do it on my own."

Case 2

Mr RP is a 73-year-old gentleman who identifies as a Torres Strait Islander (TSI). He left his family at the age of sixteen to move to Sydney to build a life of his own. Mr RP has a background of Type II Diabetes Mellitus (T2DM), from which he suffers both microvascular and macrovascular complications, including ischaemic heart disease and peripheral vascular disease. In 2005, Mr RP developed gangrenous toes on his left foot, which required trans-metatarsal amputation. Two months ago, he again developed gangrenous toes and had the fourth and fifth digits on his right foot amputated. His current hospitalisation was for hyperbaric therapy to facilitate wound healing.

A conversation with Mr RP revealed that he had little knowledge about his T2DM. The hospital staff tried educating Mr RP and providing him with information pamphlets, however Mr RP was unable to read English. He did not regularly record his blood glucose levels and was unaware that his diet was directly correlated with his diabetes and the amputation of his toes. The hospital team offered to arrange an appointment with a Diabetes Educator but this was refused.

Discussion

The above cases demonstrate a number of similarities that are important points of discussion. In case 1, Ms. NW has liver cirrhosis

from alcohol abuse; in case 2, Mr RP has T2DM with both micro- and macro-vascular complications. Both of these medical conditions are preventable with education, lifestyle changes and early intervention. Both patients are not well educated about their illness, and refused allied health and outpatient services that could help prevent further progression of their conditions.

Barriers to communication and access of services

There are many barriers that may prevent Indigenous patients from communicating freely and accessing available health-care services. These include language, cultural and historical barriers.

In the above cases, both Mr RP and Ms. NW had little knowledge about their medical conditions. Poor knowledge of one's own medical illness is not an uncommon occurrence in the Indigenous community. One Australian study showed that Indigenous patients were less certain about the cause of their illness and reported feeling uninformed but eager for information. [7]. Patients reported dissatisfaction and confusion regarding information about their illness given by doctors. Many felt confused by the advanced language of their physician. Language barriers and cultural distrust prevented them from seeking further information. Furthermore, physicians may interpret the patient's lack of questioning as indicative that their understanding is satisfactory. [7]

Fear of racism and a sense of powerlessness are examples of some of the social barriers that Indigenous patients face when having to interact with healthcare staff. In addition, cultural differences in social cues such as eye contact, body language, volume and tone of speech may hinder the therapeutic relationship. For example, lowering eye gaze when talking to people of authority is a sign of respect in Indigenous culture, while in many other cultures it may be seen as a lack of interest or defiance. [8] These miscommunications between the doctor and patient can result in lack of understanding of diagnoses and therefore poor adherence to treatment plans. Indigenous patients have reported that when they do not understand what a doctor is saying, they feel it is because the doctor does not know what she/he is talking about. Conversely, when patients understand what is being said, they feel the clinician is knowledgeable. [4]

Internationally, minority populations face many barriers to the uptake of mainstream health care services, including language and cultural barriers. Indigenous Australians are identified as a population at risk of not accessing health care services, often because of language and cultural reasons. [3] Traditional Indigenous beliefs may differ from what is practiced at the hospital; many Indigenous people are suspicious of the basic tenets of Western medicine, or "White man's" medicine. [4] For example, many Indigenous people hold the opinion that, "the ability to put on weight during good seasons enables people to survive bad seasons," and, "thinness can indicate weakness, excessive worry, or ill health." [9] Enforcing the importance of weight loss, strict calorie intake, and exercise, in conditions such as diabetes, can be difficult if patients are hesitant towards the accuracy of Western medicine or do not trust the medical professional. [9] Additionally, some Indigenous members of the Stolen Generation may choose not to see a, 'White' or non-Indigenous doctor until absolutely necessary, due to past mistrust. [5] Lack of trust in Western medicine poses a threat to compliance with medical advice and use of recommended services. It is important for culturally appropriate options to be discussed and practiced in order to increase the uptake of available services by Indigenous Australians. [3]

Impact of the doctor-patient relationship on Ms. NW and Mr RP

In the case of Ms. NW, the management team recommended a number of support services that could potentially improve Ms. NW's health outcomes. For example, support services that educate and encourage Ms. NW to adopt a healthier life style with abstinence from alcohol, maintain better nutrition and physical activity, will potentially reduce the impact of her condition on her overall wellbeing. Furthermore, providing counselling to prevent her children from engaging in risk-taking behaviour may reduce the multigenerational impact of disease.

Ms. NW was not receptive to these services and refused them from the outset. This may be due to a misunderstanding of the services or for various other reasons. The hospital treatment team rightfully offered these services, but it is unknown to what extent an effort was made to help Ms. NW understand the services. With additional efforts it may be possible to explore why she kept to herself and refused support services. However, in a busy hospital setting there are often time restrictions that may interfere with putting these additional efforts into place. Ideally, if someone she could trust and feel comfortable with explained the benefits of these services to Ms. NW in the community, for example a general practitioner (GP), there may have been better engagement and compliance leading to improved outcomes for her and her family. The importance of building a trusting doctor-patient relationship and being culturally sensitive should continue to be addressed in staff training sessions, in both hospital and community settings.

Similarly, Mr RP had refused to engage in any support services over the years and was not open to further discussion about the topic. When asked about connection to an Indigenous Liaison Officer (ILO), Mr RP's response was: "No, I don't use that kinda nonsense. I came here to get my foot fixed, and I'll get my foot fixed then leave. I lived the past 60 years on my own, I didn't need their help before and I don't need it now!" Mr RP described past occasions when people offered him services, but he refused, "I'm no different than anyone else. I don't need any special services."

Perhaps further explanation into the role and services offered by an ILO would decrease Mr RP's hesitancy towards the idea. The involvement of an Indigenous Health Worker (IHW) or ILO can positively impact patient care in many ways. By sharing the same linguistic and cultural background as their patients, ILOs can deliver effective health education to patients. Similarly they can educate other staff about Indigenous patients' needs. It is suggested that involvement of an ILO can reduce rates of discharge against medical advice amongst Indigenous patients, and also increase engagement in outpatient services. [10]

Mr RP knew little about the medical condition of T2DM, likely due to language barriers. His health outcomes may have been very different if he had been educated about the illness in his own language, early in its course. The diabetes educator and support services that were offered to Mr RP would likely have benefited him in the long term. It is unknown whether Mr RP has a GP whom he trusts, but perhaps education and advice from a trusted health care provider could help motivate Mr RP to comply with a healthier diet, exercise and other lifestyle choices, and prevent further deterioration of his condition.

Ways to enhance the doctor-patient relationship

There have been a number of proposed ways that non-Indigenous health care services can make their Indigenous patients feel comfortable, and gain trust. These include educating staff about Indigenous heritage and culture, and training them to use common terms in some Indigenous languages. [5] This has been shown to be appreciated by Indigenous patients and greatly improve rapport. [5] Having an understanding of their health and treatment options enables ownership and a 'sense of control' of their own management and can improve adherence. Displaying Indigenous artwork and employing Indigenous staff may also help Indigenous patients feel at ease and facilitate building of understanding and trust. [4]

Using simple, clear language combined with quality teaching illustrations, anatomical models, and informative CDs or DVDs may be helpful. In addition, Indigenous art and paintings about disease and health, "medical art," can be extremely useful in educating Indigenous patients about their condition. The use of a few terms in the patient's native language about their disease can aid in understanding and trust. [4]

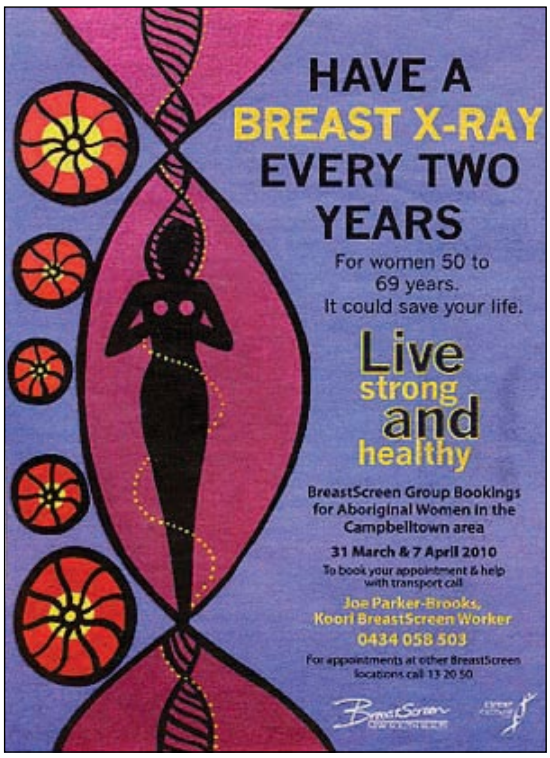

Figure 1. *This is an advertisement in a local Indigenous newspaper. [11] Targeting the Indigenous population by advertising a holistic approach to health may encourage patients to use available services.*

A study by Browne and Varcoe [12] goes one step further, arguing for a closer scrutiny of the issue of culture. They draw attention to the heterogeneity amongst Indigenous people and warn against, "painting everyone with the same brush." They urge the medical community to acknowledge individual differences and cultural diversity among Indigenous patients and make room for personal preferences. [12] The importance of building rapport and learning about the patient's background and individual beliefs, can assist the professional to understand the patient and be clear about the next steps in treatment planning. [5]

Conclusion

There has been a remarkable shift among health care providers and governing bodies to acknowledge the need for cultural sensitivity training for staff and the importance of enhancing communication with indigenous patients. Efforts to improve access to health services for Indigenous patients include cultural education, Indigenous liaison workers and the availability of interpreters. Medical training has increasingly emphasised the importance of effective communication and building rapport. Continued mindful efforts to build an empathic, trusting relationship between a doctor and a patient may go a long way in improving health outcomes for Indigenous Australians.

Consent declaration

Informed consent was obtained from both patients for publication of this case report.

Conflict of interest

None declared.

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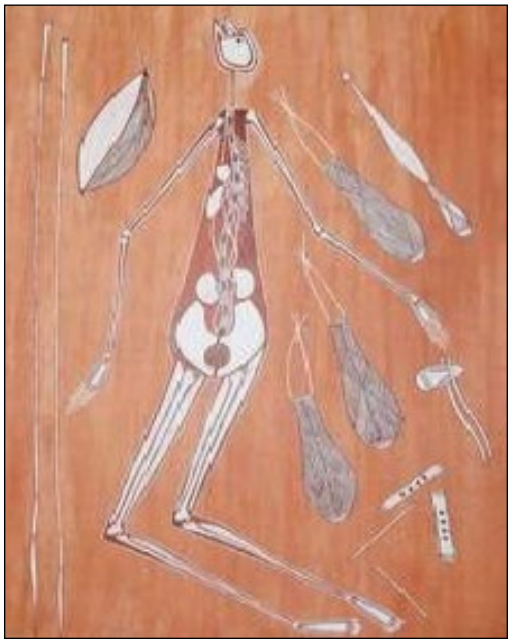

Figure 2. *This Indigenous painting shows the digestive system of the human body. Indigenous people may relate better to this kind of medical art. [11]*

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Spontaneous intracranial hypotension and postural headache

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Edward is currently studying final year medicine at the University of Notre Dame, Fremantle. He is also a registered pharmacist, having graduated from Curtin University, and he continues to practise pharmacy. His current interests lie in the fields of emergency medicine, intensive care, anaesthetics and medical education. In his spare time, he enjoys good food, travelling and spending time with family and friends.

Spontaneous intracranial hypotension (SIH) is caused by a spontaneous leak of spinal cerebrospinal fluid. Orthostatic headache is the hallmark of this condition, but due to under-recognition by clinicians and varied presentations, delays in diagnosis are common. A high degree of suspicion is required to make the diagnosis, and once confirmed by neuroimaging, it can often be managed successfully with an epidural blood patch. Novel treatments for this condition include an epidural injection of fibrin glue, with surgical repair reserved for unresponsive patients. This case report illustrates the diagnostic challenge, investigation and management of this condition. It also demonstrates the importance of relevant clinical information when interpreting imaging, and finally, aims to raise awareness of this important clinical entity.

Case presentation

A 37 year old female social worker presented to the emergency department with a three month history of intermittent headache, recently increasing in severity and duration in the last six to seven days. The headache started in the cervical spine, and curved over the head and into the face bilaterally, with a sensation of ache and pressure. Associated symptoms included nausea, vomiting, unquantifiable weight loss and intermittent auditory symptoms. Assessment by an ear, nose and throat specialist including audiometry did not reach a diagnosis. Of note, the headache was worsened when standing upright, and relieved when supine. She gave no history of prior lumbar puncture, fever, visual disturbance, numbness, paraesthesiae, weakness, urinary symptoms, vertigo or tinnitus. She had presented to her general practitioner several times and underwent a magnetic resonance imaging (MRI) brain which was reported as unremarkable. Two days prior to this presentation she attended a regional hospital Emergency Department (ED), and the next day attended a tertiary hospital ED, where she was discharged for neurology follow up. As she was incapacitated by the headaches and was struggling to care for her children while her husband worked away from home, she presented to the private ED a day later.

She had a past medical history of anxiety and depression, with symptoms well controlled on sertraline 25mg daily, prior tension headache and a past surgical history of two caesarean sections. She was taking no other regular medications and there was no relevant social or family history.

On examination, she was a young woman in no apparent distress with normal vital signs. Peripheral and cranial nerve examination, and fundoscopy were unremarkable. There were no cerebellar signs. Cervical spine examination demonstrated tenderness on palpation on the mid spine of C1 and C2, with pain on flexion and right and left lateral rotation. The remainder of the examination was unremarkable.

Clinical findings were consistent with spontaneous intracranial hypotension (SIH). She was admitted to the ward and managed on simple analgesia (paracetamol, Panadeine® and Mersyndol Forte®), temazepam and ondansetron. In light of the diagnosis, MRI brain with gadolinium and magnetic resonance venography was repeated on Day One. This demonstrated features consistent with intracranial hypotension: inferior descent of the cerebellar tonsils through the foramen magnum (Chiari 1 malformation), reduction in the suprasellar cistern, bilateral shallow subdural hygromas over both convexities and mild diffuse dural enhancement within the supratentorial location. A magnetic resonance venogram demonstrated patent dural venous sinuses. MRI cervical spine demonstrated a small volume of fluid between the posterior elements of C1 and C2 which was extradural in location. Cervical spine degeneration was described without cord compression, and there was some mild foraminal narrowing bilaterally at C5/C6.

Admitted under the general physician, she was reviewed by the neurologist on Day Three, who recommended a MRI of the thoracic and lumbar spine. This demonstrated degenerative changes of discs but failed to identify the location of the leak. As such, a lumbar epidural blood patch was performed by the anaesthetist on Day Five. Follow up on Day Six was normal, and she was discharged with advice to contact her neurologist for any further issues. When followed up four months later, she was asymptomatic and satisfied with the outcome. She was also able to return to full activities.

Discussion

Intracranial hypotension is defined as an abnormally low intracranial pressure (normal 10-15mmHg), and is characterised by headaches exacerbated by standing and relieved when supine. [1,2] Spontaneous intracranial hypotension is caused by spontaneous leakage of cerebrospinal fluid (CSF) through the dura mater. Whilst it is an important cause of new headaches in young and middle-aged individuals, it is not well recognised, leading to misdiagnosis, significant delays or never being diagnosed. [3] Initially described by Georg Schaltenbrand in 1938, this eponym has fallen out of favour due to his role in the Third Reich. [1,4,5] The prevalence has been estimated at 1 per 50,000 headache presentations in an emergency department study, with a female preponderance (male to female ratio of approximately 1:2). [6] Symptoms typically occur in the 40s and 50s with a peak incidence around 40. [3]

The exact aetiology often eludes discovery, but two contributing factors that are frequently suspected include weakness of the meningeal sac in certain regions and trivial traumatic injury (in about one third of patients). [3,7] Other predisposing factors include individuals with underlying connective tissue disorders, such as Marfan syndrome, Ehlers-Danlos syndrome type II and autosomal dominant polycystic kidney disease, as these increase the likelihood of CSF leak from

spontaneous dural tears or the formation of meningeal diverticula. [3,8] Other causes of localised defects of the connective tissue, such as vertebral spurs, and dural rents and tears have been observed during surgery. [8] Symptomatic causes such as spontaneous CSF rhinorrhoea or otorrhoea, uraemia or diabetic coma are less common and the obvious clinical presentation facilitates the diagnosis. [1] Uncommon causes involving the piercing of the dura include osseous spinal pathology caused by congenital defects or acquired degenerative disc disease.[8]

Leak of CSF at a spinal level causes CSF hypovolaemia, resulting in a reduction in brain buoyancy. This causes sagging of the brain in the cranial vault and stretching of pain-sensitive structures, such as the venous sinuses around the brain, the blood vessels of the meninges and the dura mater, accounting for the characteristic postural symptoms. [8,9] Vascular congestion may also contribute to the headache. [8] Physiological compensation is explained by the Munroe-Kellie hypothesis, which states that the sum of volumes of brain, CSF and intracranial blood is constant. Thus a decrease in one should cause an increase in one or both of the remaining two. [10] In response to CSF hypovolaemia, there is an increase in the vascular component (by dilatation of compliant intracranial blood vessels) as the volume of brain parenchyma remains constant. [8] In addition, hygromas may form to restore depleted intracranial volume. Therefore CSF hypovolaemia has been proposed as the underlying mechanism for the headache syndrome, as opposed to CSF hypotension per se. [11]

The diagnosis of SIH is challenging due to the variability in headache symptoms and the lack of awareness by clinicians. This diagnosis should be considered in patients presenting with a postural headache or a daily persistent headache without an alternative cause. The hallmark of this condition is a postural headache that occurs or worsens within 15 minutes of assuming an upright position, and improves rapidly, usually within 15 to 30 minutes, of assuming a recumbent position. In some patients, however, the time period before the onset of the headache may be as long as several hours. Patients in the chronic phase may experience resolution of the headache but persistence of other symptoms. In rare cases, postural headache may not be experienced, even at the outset. In some, the headache becomes persistent rather than postural. [3,8,12,13]

The onset of headache may be gradual or sudden, and rarely starts as a thunderclap headache, which is seen in subarachnoid haemorrhage. It is often described as generalised and throbbing in character, but may be reported as dull or focal involving the frontal or occipital region. The severity of the headache varies from mild to incapacitating. Other exacerbating factors include head movement, straining, coughing, sneezing, jugular venous compression and high altitude. Other clinical manifestations include back pain, radicular symptoms, postural neck discomfort, nausea, vomiting, dizziness, vertigo, gait unsteadiness, ataxia, blurred vision, photophobia, transient visual obscurations and diplopia attributable to cranial nerve VI palsy. Hearing disturbance due to traction on the cochlear nerve or abnormal intra-labyrinthine pressure may cause tinnitus or hypoascusis (reduced sensitivity to sounds). [3,8,12,13]

Infrequently, more severe neurological manifestations occur, including Parkinsonism, quadriparesis and cerebellar haemorrhage. Pituitary congestion and enlargement may cause hyperprolactinaemia and galactorrhoea. Patients may also present with subtle cognitive deficits or coma. Notably, most of the neurological deficits are reversible following treatment. [3,8,12,13]

Neuroimaging, particularly MRI, is of great utility in establishing a diagnosis and identifying the site for later intervention. Major MRI findings with gadolinium enhancement include subdural fluid collections, enhancement of the pachymeninges with leptomeningeal sparing, engorgement of the venous structures, pituitary enlargement and sagging of the brain with cerebellar tonsillar herniation. Other findings include a decrease in the size of cisterns and ventricles, pituitary hyperaemia, swelling of the upper brain stem, effacement of the prepontine cisterns, descent of the cerebellar tonsils resembling Chiari 1 malformation, subdural haematomas (in up to 20%) and subdural hygromas. [8,13,14]

Computed tomographic (CT) myelography and Gadolinium-enhanced MRI may be used to identify the site of the leak. MRI scans may be normal in up to 20% of patients, and radionucleotide cisternography may be used to detect a leak instead. A brain CT is usually normal, but may demonstrate slit-like ventricles or tightness of the basal cisterns, and subdural hygromas. Prior to the recognition of characteristic MRI findings, lumbar puncture was the study of choice. Findings included low CSF opening pressure, but this could appear normal despite CSF hypovolaemia on neuroimaging. This may have been due to prolonged recumbency or an intermittent leak. Rarely, an inability to obtain CSF may be experienced. Other CSF studies are usually normal, but mildly raised protein and a reactive pleocytosis may be demonstrated. [8,13,14]

In one case series, 42% of patients managed conservatively (including bed rest, oral or intravenous hydration, analgesia and 200 to 300mg of caffeine orally twice to three times a day) recovered. [8,15] Adjuncts include abdominal binders (which may help some) and glucocorticoids (some benefit reported but it is yet to be proven). The duration of conservative treatment before the decision for other intervention is made on a case by case basis. [3,8]

Epidural blood patch (EBP) is currently the mainstay of treatment, and involves 10 to 20mL of autologous blood injected into the epidural space. [8] The success of the first patch varies (36-57%), with targeted epidural blood patch being more effective. [7,16] The mechanism of the EBP is believed to be the spread of blindly patched blood through the lumbar route. This may then spread to the cervico-thoracic level when the patient is in the Trendelenburg position, plugging the dural rent. The fibrin reaction at the site of the leak forms a scar in two to three weeks. A tamponade effect is provided and causes some degree of restoration in the CSF volume, resulting in symptomatic relief. Small retrospective studies and case series demonstrate that more than one EBP is required in at least 50% of cases. If the second patch fails, neuroimaging is used to visualise the leak and a targeted blood patch is applied. This has been shown to be more effective than blind EBPs. [8,16] A novel technique using a double EBP at two different levels (lumbar and thoracic) in the same procedure has been described for cases of SIH without a clear, demonstrable CSF leak. [17] Further studies are required to gauge the value of this technique.

Surgical repair is the last resort, and is reserved for patients who fail to respond to conservative management and blood patches. There is close to 100% success rate for meningeal diverticulae treated by simple ligation and repair of meningeal tears. [13] Novel treatment modalities include an epidural injection of fibrin glue for patients unresponsive to an epidural blood patch. Epidural saline infusion has also been attempted, producing immediate relief albeit with reduced efficacy. [13] Finally, patients with a long history of the disease may develop chronic headache syndromes. This pain is unrelated to posture, but is highly refractory to analgesia. [18]

Conclusion

Spontaneous intracranial hypotension is an important cause of new onset headache in young and middle-aged individuals. A detailed history and examination can alert the clinician to include this condition in the differential diagnosis. Subsequent investigation with neuroimaging provides a sensitive diagnostic test, and may locate the site of the leak. Treatment is often conservative or with an epidural blood patch, leading to complete resolution of symptoms in the majority of patients. SIH is frequently overlooked as a cause of headache. An increased awareness of this condition would provide earlier diagnosis and significant improvement in quality of life for these patients.

Consent declaration

Informed consent was obtained from the patient/next-of-kin for publication of this case report and accompanying figures.

Conflict of interest

None declared.

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Physician Assistants in Australia: the solution to workforce woes?

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This article reviews the potential for Physician Assistants (PAs) within Australia. An introduction to the PA role, training, and relevant history is included, as is motivation for considering implementation of the role within Australia. It specifically addresses the prospect of improving rural and Indigenous health services. The possible impact on other roles within Australia, including Nurse Practitioners and medical students, is also considered. Finally, it is concluded that larger trials are required to adequately assess the benefit of the profession to Australia.

Introduction to Physician Assistants

With the recent suspension of the Physician Assistant (PA) training programme at The University of Queensland, and reservations expressed by nursing and medical organisations, there is potential for ambiguity regarding the prospects of the profession in Australia. [1,2] Whilst the concept is relatively new to the country, it is well-established internationally, [3] and in the United States has mitigated certain deficits in health service provision. [4]

A PA is a licensed medical professional who operates within a set scope of practice under the authority of a supervising doctor. [5] Whilst they may complete tasks independently, the supervising doctor has final responsibility for the PA and the clinical care they provide. [4] The role is not designed to serve as an independent practitioner. [4] Thus, a PA's scope of practice can vary significantly, depending on the health facility at which they are employed, the extent of further training undertaken, and the degree of clinical autonomy the supervising doctor is willing to allow. [4]

The concept of the PA was introduced in the 1960s in response to both a shortage and uneven geographic distribution of doctors within the United States. [4,6] The founder of the PA movement, Eugene Stead, initially intended an advanced nursing programme. However, the National League of Nursing rejected this proposal, prompting the utilisation of trained military medics as the pioneering class. [7] The first cohort of PAs graduated in 1967, [8] and since then a large number of tertiary institutions have commenced training programmes. [4]

Entry into training programmes is competitive, with at least two years of university study usually required as a pre-requisite. [4] Most candidates also have at least four years prior experience in a medically related field, having transitioned from allied health and nursing careers. [1,4] PAs train for an average of twenty-five months in a course now typically designed as a Masters level programme, representing an abridged version of traditional tertiary medical education. [4] Similar to other medical professionals, PAs are required to undergo continuing professional education and meet recertification requirements. [8] In the United States, the recertification period is currently six years, although this will be transitioning to ten years from 2014. [9]

The role of PAs includes taking patient histories, performing clinical exams, diagnostics, patient education, basic procedural work such as suturing, and providing general assistance to doctors as required. [4] PAs may also complete more advanced tasks under the delegated authority of doctors, including endoscopy, critical care, and specialist outpatient clinics. [10-12] Importantly, evidence shows that in specific clinical situations PAs can provide a level of care comparable to doctors. [4]

The significance of the PA role to the United States health care system is clear, with over seventy thousand practising in 2010. The profession has expanded consistently since 1991, with graduates from over 150 accredited training facilities set to see in excess of ninety thousand PAs in the United States by 2014. Growth in the profession is predicted to continue, with numbers estimated to exceed 125 000 by 2025. [13]

Motivation for considering the role in Australia

The PA role has been discussed as a potential solution to problems facing the medical workforce in Australia and, although small in size, results of trials in Queensland and South Australia have been encouraging. [12,14] The 2008 Parliamentary Library report and 2011 Health Work Force Australia report have also recommended the profession be considered given the challenges facing medical care in Australia. [12,14] An ageing population, increased patient expectations and the burden of chronic disease all place considerable strain on a system already understaffed, whose employees are demanding more work-life balance than before. [15,16] The size of this problem is clear, with estimates that by 2025 over twenty percent of the total workforce in Australia would need to be employed in the health system to maintain services at their current level. [17] The response has been to increase medical graduate numbers and recruit doctors internationally, yet with demand set to exceed supply, PAs represent a possible solution to Australia's expanding medical workforce requirements. [18] Arguments have also been made that PAs could decrease Australia's reliance on International Medical Graduates (IMGs), which would be a move toward "self reliance" as recommend by the National Health Workforce Strategic Framework in 2004. [19,20]

Although the workforce shortage is a serious issue, perhaps a greater concern is the financial sustainability of the health care system. In 2009, approximately ten percent of Australia's Gross Domestic Product (GDP) was spent on health care. [19] This is expected to growth at a rate of 0.5% per year, meaning health expenditure will account for twenty percent of Australia's GDP by 2020. [19] Therefore, in an effort to achieve sustainability, avenues to mitigate this rising financial burden must be explored. This provides motivation to consider the PA role within Australia, especially given evidence demonstrating their potential cost-effectiveness. [18,21-23]

The 2011 Health Work Force Australia report indicated a number of possible roles for PAs in Australia, including providing services that have traditionally been the sole domain of doctors. [1] Whilst this may seem like a new paradigm, the concept of dispersing such

knowledge and expertise amongst various members of the health workforce is not new to Australia. Such change can already be seen in the medical profession with the development of General Practitioner (GP) proceduralists who, particularly in rural areas, perform tasks previously only completed by specialists. [24] This dynamic practice has been essential to ensuring service viability in rural areas, including maintaining obstetric services. [24] Paramedics have also been shifting towards a more professional role, utilising expanded skills bases, and in some instances having admission rights to hospitals. [25,26] The Nurse Practitioner (NP) role has also expanded within Australia, and NPs now complete extended patient assessments, prescribe certain items independently, and collaborate with doctors where required. [27] Whilst there are some reservations about the expanding scope of practice for non-doctor roles, the success of such redistribution of tasks in Australia provides motivation to review the way in which medical care is provided. [28] However, to ensure quality of care and patient safety, this should continue forward with consultation from appropriate medical governing bodies. [27,29]

The potential role of Physician Assistants in rural Australia

Rural communities in Australia currently experience significant disadvantage in accessing health care, with staffing shortages being exacerbated by an uneven distribution of practitioners that favours metropolitan areas. [2] This issue is set to be compounded by an ageing rural workforce and resultant practitioner retirement. [1] To a large extent IMGs have helped minimise this effect, with over half of doctors working in areas classified as small rural to remote being trained internationally. [2] However, evidence suggests that IMGs bonded to work in rural Australia tend to be dissatisfied both personally and professionally, [30] demonstrating a clear need to find a sustainable rural health workforce. This provides a perfect niche to utilise PAs, with some research in the United States showing that as a profession PAs may be more willing than doctors to move to areas of need, including rural locations. [18] Such use of PAs to mitigate rural health workforce shortages is supported by both the Australian College of Rural and Remote Medicine and the National Rural Health Alliance. [18]

In an Australian rural pilot trial in Cooktown, PAs significantly reduced the requirement for doctor overtime despite increased caseload. This shows potential to reduce doctor fatigue and consequently the rural attrition rate, which is essential to ensure continued viability of rural health services. [14] The potential benefit of PAs was further seen in a Mt. Isa trial, which coincided with an H1N1 outbreak. During this time period, PAs conducted a fast-tracked clinic to decrease the burden on emergency physicians. [14] The benefit of their input continued over the following months, with Emergency Department presentations, particularly in the lower triage categories, decreasing following initiation of a PA-led primary care clinic. [14]

Furthermore, PAs have the potential to improve Indigenous health services. In the Queensland pilot, PAs at Wujal Wujal, Karumba and Normanton at times worked under remote delegation, improving access of the local Indigenous community to health professionals. [2] If expanded, this could yield an important step forward in health equity by ensuring that medical professionals are on-site to deliver the services these areas require. However, patient feedback regarding this service was difficult to obtain, with very few Aboriginal and Torres Strait Islander (ATSI) patients completing the feedback survey. [2] Scope of practice for PAs at one trial site was also restricted for ATSI children, requiring approval from a supervising physician before initiation of any therapy for patients below a pre-determined age. This was prophylactic rather than in response to any actual breach of care, on the basis that presentations of children in this group often do not reflect the true breadth of underlying illness. [2] It should, however, be remembered that PAs participating in the trial were trained internationally. If PAs were trained locally in programmes designed to meet the health needs of Australian populations, such measures are unlikely to be necessary.

The Queensland PA trials yielded no safety or treatment concerns over twelve months. However, due to their size, limited analysis, and issues regarding scope of practice, the benefit of the role to the local health system was unable to be completely established. Therefore, given the potential utility, further study should be completed to demonstrate if PAs can adequately address the rural and Indigenous workforce shortage. For these trials to adequately assess the role in rural Australia, implementation of a proper support network and a change in legislation, particularly surrounding prescribing rights, would be required. [14,31]

Further potential roles of Physician Assistants in Australia

PAs could also increase the capacity of procedural units by taking responsibility for low-risk routine tasks such as endoscopy, running specialised outpatient clinics, and providing early assessment of new cases in emergency departments, allowing doctors to focus on more complex tasks. [2,10,18] The same is true of general practice, where PAs have been shown capable of managing the majority of minor cases to a similar level of care as GPs. [32] In a recent United Kingdom-based study, PAs were shown to expand the capacity of trial sites to provide primary care to their local population. [32] Specific tasks performed by PAs in this trial included follow up of laboratory results, basic procedural work, completing PAP smears, and patient education. One major difficulty encountered was the inability to prescribe under current legislation, which has also been reflected in Australian trials. [32]

Concerns regarding impact on other roles in the Australian health care system

Concerns have been voiced that PAs may encroach on the role currently held by Nurse Practitioners (NPs) including the Rural and Isolated Practice Registered Nurse role, which was specifically designed to meet rural needs. [2,31] Counter-arguments have been made that the NP role is protocol-driven and based on a nursing model of care, whilst the PA role is based on the medical model with a greater emphasis on diagnostics; therefore, unique roles for both professions could be determined. [2] Despite this, the overlap between the two roles is significant. [5,14,38] As such, further trials of PAs must examine the impact on the NP profession, which is now well-developed within Australia. [2]

In terms of quality of care, numerous studies have shown that in certain areas of clinical practice, NPs, PAs and doctors achieve similar clinical outcomes and a similar degree of patient satisfaction. [4, 34-38] Therefore, given the proven NP role, unless evidence is produced demonstrating enhanced quality of care or ability to undertake tasks not performed by NPs, the cost of implementing this profession in Australia's health care system cannot be justified. Even if such novel roles or quality addition could be proven, the cost of introducing and sustaining PAs including physician supervision demands careful cost-benefit analysis. [31] This is particularly important in the current era of unsustainable medical expenditure. Furthermore, as Australia continues to face a so-called "tsunami" of medical students, the requirement for further low- to mid-level clinical roles, particularly those not yet well-established, must be seriously reviewed.

The effect on physician and medical student training must also be determined, particularly given the increased numbers of medical graduates. The National Health Workforce Taskforce report illustrated the extent of this problem, estimating that in comparison to 2005, in 2013 over 600 000 more medical placement days per annum will be required to train undergraduates. [2] Therefore, as the role of PAs is examined, it is essential to ensure junior doctor and medical student training is not impaired. There are as-yet unsubstantiated claims that PAs may allow more time for senior clinicians to teach. [2,14] However, more research and consideration into this as it applies to the Australian context is warranted. [2] This is particularly important as, despite large increases in the numbers of medical graduates, a significant proportion

of senior consultants are approaching retirement age. [39] This may lead to diminished clinical exposure for medical students, a situation which could be further exacerbated should consultants also be tasked with fulfilling PA teaching and ongoing supervision requirements. This is an issue already considered in the Queensland pilot trials, where PA scope of practice for certain procedural skills was limited to ensure junior doctors gained the necessary experience. [2]

Conclusion

Trials in Australia regarding PAs have been limited and utilised internationally-trained recruits with proven clinical acumen. [2,12,14] Therefore, despite encouraging results, larger trials are required to determine their potential to benefit the Australian health care system. Even if the conclusion was drawn that the implementation of PAs was the best way to meet the requirements of the Australian health care system, there are still multiple barriers that would need to be addressed. These include setting up appropriate prescribing rights under the Pharmaceutical Benefits Scheme, without which their effectiveness would be severely limited. [12] The potential for roles in rural and remote communities and procedural work seems encouraging. [2,17] However, concerns regarding the impact on the proven NP role and medical student training must be addressed in further trials before conclusions can be drawn on the wider impact of implementation in Australia. [2,31]

Conflict of interest

None declared.

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The role of Aboriginal Community Controlled Health Services in Indigenous health

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"Our right to take back responsibility." Noel Pearson, 2000 [1]

This emotive aphorism by Pearson embodies the struggle of Australia's Indigenous people to gain control of their destiny, which for generations has been wrested from them into the power of governments. Although his statement was primarily directed toward welfare, the same right of responsibility can be applied to health, perhaps the gravest challenge facing the Aboriginal population. As Pearson alluded to, the only way to solve the health crisis is by enabling local communities to take charge of their own affairs. This principle of self-determination has led to the creation of Aboriginal Community Controlled Health Services (ACCHS), which has allowed over 150 Aboriginal communities throughout Australia control over their healthcare. [2] This article describes the founding principles behind community controlled health centres in Aboriginal communities through considering several different ACCHS and the unique challenges they face.

The fundamental concept behind each ACCHS – whether metropolitan, rural or remote – is the establishment of a primary healthcare facility that is both built and run by the local Aboriginal people "to deliver holistic, comprehensive, and culturally appropriate health care to the community which controls it." [2] This is based upon the principle of self-determination and grants local people the power to achieve their own goals. From the beginning ACCHS were always intended to be more than exclusively a healthcare centre and each ACCHS has four key roles: the provision of primary clinical care, community support, special needs programmes, and advocacy.

ACCHS endeavour to provide primary healthcare as enshrined by the World Health Organization in the 1978 Declaration of Alma-Ata. This landmark international conference defined primary healthcare as:

> "essential health care based on practical, scientifically sound and socially acceptable methods and technology made universally accessible to individuals and families in the community through their full participation and at a cost that the community and the country can afford to maintain… in the spirit of self-determination." [3]

Although conceived subsequent to the advent of the community controlled healthcare movement in Australia, this definition echoes many of the underlying principles upon which ACCHS were founded, including the most important aspect – local control. Indeed, it is widely accepted throughout the literature that the community itself must identify its needs and problems so an effective and appropriate course of action can be undertaken. [4-7]

This principle is espoused in the National Aboriginal Health Strategy's frequently quoted statement that "Aboriginal health is not just the physical well-being of an individual but the social, emotional and cultural well-being of the whole community in which each individual is able to achieve their full potential thereby bringing about the total well-being of their community." [8] The notion of 'community' is an essential component of the Indigenous view of the self and therefore strongly related to health and well-being. Accordingly, ACCHS have a holistic view of healthcare, recognising that Indigenous healthcare needs to be multi-faceted and focus on cultural complexities that may not be appreciated by mainstream health services. As each Aboriginal community across the country has a distinct culture and language, [9] local control is paramount.

The concept of community control is not new. It can be traced back to early nineteenth-century America, where such services were used with success for improving the health of the poor and recent migrants. [4] The first ACCHS was established in the inner city Sydney suburb of Redfern in 1971. [10] Known as the Aboriginal Medical Service (AMS), it pioneered the concept of community controlled healthcare in Australia and, from modest beginnings, has now expanded into a major, versatile healthcare facility that provides free medical, dental, psychological, antenatal and drug and alcohol services to the large Aboriginal community in Sydney. Redfern's AMS overcame struggles against an initially distrustful and paternalistic government through the dedication of visionary Indigenous leaders and support of benevolent non-Indigenous Australians. [10,11]

Specialised Indigenous policies are essential, as it is impossible to apply the same approach that is used in health services for non-Indigenous patients. Many Indigenous people are uncomfortable with seeking medical help at hospitals or general practices and therefore are reluctant to obtain essential care. [12] In addition, access to healthcare is often extremely difficult due to either geographical isolation or lack of transportation. Many Indigenous people live below the poverty line, so the services provided by practices that do not bulk bill are unattainable. Mainstream services struggle to provide appropriate healthcare to Aboriginal patients due to significant cultural and language disparities; [5,13] the establishment of ACCHS attempts to overcome such challenges.

For example, the Inala Indigenous Health Service in south-west Brisbane performed extensive market research to determine the factors keeping Aboriginal patients from utilising the mainstream health service. The results showed that several simple measures were highly effective in engaging the local community, such as employing an Indigenous receptionist and making the waiting room more culturally appropriate through local art or broadcasting an Aboriginal radio station. [12] In the five years following implementation of these strategies, the number of Indigenous patients at Inala ballooned from 12 to 899, and an average of four consultations per patient per year was attained, compared to the national Indigenous average of fewer than two. [14] A follow-up survey attributed patient satisfaction to the presence of Indigenous staff and a focus on Indigenous health. [12]

Nevertheless, the consequence of longstanding obstacles to Indigenous access to mainstream healthcare is manifest in the stark inequity between the health outcomes of Indigenous and non-Indigenous Australians. The most recent data from the Australian Institute

of Health and Welfare (AIHW) shows that the discrepancy in life expectancy between Aboriginal Australians and their non-Indigenous counterparts remains unacceptably high, at 11.5 years for males and 9.7 for females. [15] Moreover, studies demonstrate that Aboriginal people have significantly worse outcomes in key health indicators, including infant mortality, diabetes, heart disease, infectious disease and mental illness. [5,12,13,16] Such disparities indicate that a novel, tailored approach to Indigenous health is required.

Cultural understanding is essential, as demonstrated by the example of the Anyinginyi Health Aboriginal Corporation in the Northern Territory. Anyinginyi serves the twelve remote Aboriginal communities within a 100km radius of Tennant Creek and its name comes from the local Warumungu language, meaning 'belonging to us' [17] emphasising the community's control of, and pride in, this service. Anyinginyi has always strived to be more than just a health service and has evolved to deliver many other community programmes. This is embodied by Anyinginyi's insistence on 'culturally appropriate' healthcare for Aboriginal people. In addition to medical advice, the local Aboriginal community is offered support through various programmes that range from employment services to cultural and spiritual activities promoting Indigenous language and culture. One such social service is the 'Piliyintinji-Ki Stronger Families' initiative, which assists community members through access to support services relating to issues such as family violence and the Stolen Generations. [17] Indeed, ACCHS such as Anyinginyi have the additional benefit of providing employment opportunities for community members, as the vast majority of the employees are Indigenous. All new staff members participate in a Cross Cultural Workshop, as one of Anyinginyi's goals is to ensure that the local Aboriginal cultures are respected and continue to thrive.

The other important arm of healthcare in ACCHS relates to population health, with initiatives ranging from education campaigns to immunisations and screening for diseases. [2] One of the first large-scale community health promotion campaigns run specifically for Aboriginal people was conducted by the Redfern AMS between 1983-1984 to encourage breast-feeding among the local Koori mothers. [11] It achieved such stunning success that it set a precedent for all future ACCHS to continue in the important area of preventative medicine, with similar campaigns for sexual health and safe alcohol consumption having been undertaken subsequently.

Moreover, each ACCHS runs special services that are dictated by local needs and priorities. In some instances, there is a specific health problem that needs to be addressed, such as poor nutrition or substance abuse. Other programmes are directed at specific groups, such as young mothers or the elderly. The flexibility of these special services allows each ACCHS to identify and address the most significant problems within its area – problems that can only be identified by the community itself. For example, the Danila Dilba Health Service in Darwin runs a programme called 'Dare to Dream' that provides support and counselling for young Indigenous people suffering from mental illness. [18] It is an early intervention programme that intends to identify and support adolescents exhibiting early signs of both behavioural and mental health problems. To this end, school visits are undertaken to promote awareness of mental health issues to students and staff, as well as the services that Danila Dilba has to offer. A 'chillout' centre has been set up in Darwin as a safe place for young people to come and allows the community workers to refer those who present to appropriate counselling services. As such, Danila Dilba is empowered to proactively address an important local issue in the most culturally-appropriate way.

ACCHS are also active in the area of advocacy. This involves providing a voice for the community so that their needs can be expressed. Although each ACCHS operates autonomously, they form a national network with their collective interests represented both on a state/territory level and also nationally. Each of the eight states and territories has a peak representative body that acts on behalf of all ACCHS within that jurisdiction. [2] Examples of these organisations include the Aboriginal Health & Medical Research Council of New South Wales and the Aboriginal Medical Services Alliance Northern Territory. At the national level the umbrella body overseeing all the different stakeholders across the country is the National Aboriginal Community Controlled Health Organisation (NACCHO). [2] Individual ACCHS, as well as NACCHO and the affiliated state or territory peak bodies, lobby all levels of government for increased funding and greater recognition of the issues facing Aboriginal communities. The collective weight of NACCHO as a national advocate allows each community's needs to be heard.

Inevitably, the scope of the services each ACCHS can provide is restricted by funding, most of which comes from the Commonwealth or State and Territory Governments. [2] More money continues to be spent per capita on mainstream health services than on Aboriginal health, despite the great dichotomy in health outcomes. Indeed, the 2012 Indigenous Expenditure Report published figures showing that for every dollar spent on healthcare subsidies for non-Indigenous health, only $0.66 is spent on Aboriginal health. [19] This statistic covers all the key areas of healthcare expenditure, such as Medicare rebates, the pharmaceutical benefits scheme (PBS) and private health insurance rebates. Therefore, Indigenous patients are not receiving the same level of health service delivery, including clinical consultations and treatment, compared to their non-Indigenous counterparts. However, it is propitious to note that the funding bodies have recognised the value of the public health efforts of ACCHS, as the spending in this area is a $4.89 to $1.00 ratio in favour of Indigenous health. [19] Nevertheless, the priority needs to be placed on ensuring that sufficient funding exists to allow Indigenous patients to access health care subsidies as required.

In addition to inadequate funding, another major obstacle that ACCHS face is the difficulty in attracting and retaining doctors and allied health professionals. According to the AIHW's most recent report, only 63% of Indigenous health services currently employ a doctor. [20] Consequently, a significant increase in the number of general practitioners working with Indigenous patients is required simply to provide adequate services. There is additionally a severe lack of Aboriginal medical students and general practitioners, which limits the opportunities for Indigenous professionals to provide culturally-appropriate care to their own communities. Census data from 2006 found that there were 106 Indigenous doctors nationally, accounting for only 0.19% of all medical practitioners. [21] These shortages are compounded further for ACCHS in rural and remote areas. By 2011, further data from Medical Deans demonstrated that the numbers had increased to 153 Indigenous medical practitioners nationally, along with 218 enrolled Indigenous medical students. Although promising, these numbers remain grossly inadequate to fulfil workforce demand. [22]

Services become stretched due to perpetual resource inadequacies. Understandably, the remoteness of some communities makes service delivery challenging, yet even major metropolitan areas with large Indigenous populations can struggle to adequately provide for those in their catchment area. Under-resourcing places major constraints on service delivery and different ACCHS throughout the country exhibit significant variation in the level of services offered. Some are large, employ several doctors and provide a wide range of services; others are much smaller and operate without doctors. [20] These rely on Aboriginal health workers and nurses to provide the bulk of primary healthcare.

As such, the success of the ACCHS concept would not have been possible without the contribution of Aboriginal health workers. The role of Aboriginal health workers, who are often sourced from the local community, is to provide the primary healthcare that ACCHS offer. [23] This involves assessing patients and then coordinating or providing the medical attention required. Health workers are able to treat certain conditions with the help of standard treatment guidelines and provide a selection of important medications to patients. Importantly,

Aboriginal health workers have a liaison role between medical professionals and Aboriginal patients. They are often required to act as an interpreter between the patient and health professional, thus providing an intermediary for cross-cultural interactions, and therefore improving the quality of healthcare provided to the local community.

Due to the often quite remote locations of ACCHS and the scarcity of doctors and nurses, Aboriginal health workers perform many clinical tasks that would be provided by a medical professional in mainstream health services. Aboriginal health workers bear much greater responsibility than their colleagues in the public sector and often learn a wide range of procedural skills including how to perform standard health checks, vaccinations and venepuncture. [23] Indeed, some choose to specialise in a specific area (such as diabetes, pregnancy or infant care) thus gaining additional skills and responsibilities. Still others take on managerial responsibilities. This is in contrast to the public sector, where health workers are often fixed to one routine area or even to non-clinical work such as transportation or social assistance. [23] Without Aboriginal health workers performing these additional tasks, ACCHS would not be able to provide a sufficient level of service for the community. For this reason, Aboriginal health workers are rightly considered the backbone of community controlled health services.

As one example, the Pika Wiya Health Service in the South Australian town of Port Augusta runs two outreach clinics for communities in Copely and Nepabunna. Due to the shortage of doctors, these clinics are staffed entirely by Aboriginal health workers. Their invaluable contribution is evident, with 695 clinical encounters performed by health workers during 2008, [24] ensuring that the absence of doctors did not deny the local people the chance to receive healthcare. Whilst the major health issues faced by Indigenous people are broadly similar between urban and remote communities, these problems are often compounded by the remoteness of the location. Although these are challenges that Copely and Nepabunna will continue to have to face, the empowerment of Aboriginal health workers has helped redefine the direction of Pika Wiya's outreach health services.

Aboriginal health workers face many difficulties. Perhaps the most significant is that, until recently, there had been no national qualifications or recognition of the skills they developed. [23] The introduction of national registration for Aboriginal health workers (from July 1 2012) and the new qualification of Certificate IV in Aboriginal and Torres Strait Islander Primary Health Care (Practice) have revolutionised the industry. [25] This has had the benefit of standardising the quality and safety of the Aboriginal health worker labour force. However, as the changes will increase the required length and standard of training, there is the potential for current or prospective health workers to be deterred by the prospect of undertaking study at a tertiary level, particularly if they have had limited previous education. Nevertheless, national registration is a positive step for recognising the important work done by Aboriginal health workers, and in providing them with the training to continue serving their communities.

In addition to doctors, nurses and health workers, medical students are also important stakeholders in Indigenous health. First, much has been done in recent years to increase the numbers of Indigenous medical students. For example, the University of Newcastle has been the first medical school to make a dedicated attempt at training Indigenous doctors and has produced approximately 60% of Australia's Indigenous medical practitioners. [26] This achievement has been based on a "strong focus on community, equity and engagement by the medical profession." [26] Encouraging community members to enter the profession can be an important way of addressing both the lack of doctors in Indigenous communities and paucity of doctors of Indigenous background. The benefits are broader than this, as Indigenous doctors provide strong role models for young Indigenous people and also have the opportunity to contribute with advocacy and leadership within Indigenous health.

Secondly, the medical student population as a whole is exposed to increasingly more Indigenous health as part of the core curriculum at university following adoption of the updated Australian Medical Council accreditation standards from 2007. [27] Additionally, some students even have the opportunity to spend time in an ACCHS and experience first-hand how the system works. There has been some criticism of these 'fly in, fly out' medical electives, where students are sent to ACCHS for short periods and then leave. [28] Whilst this model may be beneficial for the student, it fails to engage the local community as they are unable to build meaningful or lasting relationships with the student.

Better models allow for a longer-term placement and immersion in the community. These include the John Flynn Placement Programme where some students are able to spend a fortnight annually in an ACCHS in the Northern Territory over a period of four years. [29] Another example is the Northern Territory Clinical School, which allows third-year medical students from Flinders University to spend a whole year of study in Darwin, providing the opportunity for increased contact with local Indigenous communities. [30] Initiatives such as these help to build a relationship with the community, and allows for increased acceptance of the medical student. Additionally, the student is able to make a more meaningful contribution to various client's healthcare. Prolonged or longitudinal attachments have also been shown to increase the likelihood of students returning as a doctor. [31] Certainly, there is much scope for the contribution of medical students to be harnessed more effectively.

It is abundantly apparent that any solution to address the health inequalities of Aboriginal people will only be effective if it recognises that the local Aboriginal communities must control the process of healthcare delivery. This is the principle upon which ACCHS were founded and can be attributed to their many successes, as demonstrated through the examples of Redfern's AMS, Inala, Anyinginyi, Danila Dilba and Pika Wiya. In spite of the challenges posed by inadequate funding, under-staffing and often remote locations, these organisations strive to uphold the ideals of self-determination and community control. It is hoped that wider adoption of these principles by national governing bodies together with improved financial support will enable Indigenous Australians control over their lives and destinies, leading to better health outcomes.

Conflict of interest

None declared.

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The history of breast cancer surgery: Halsted's radical mastectomy and beyond

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Breast cancer is common. One in eight Australian women will be diagnosed by the time they turn 85, and it has been estimated that this year in Australia approximately 14,600 women will receive the diagnosis, around 40 women each day. [1] A significant proportion will undergo surgery, mostly as the first means of treatment. Over the past forty years many advances have been made in the surgical approach to breast cancer. [2] New techniques and approaches have been developed and efforts for further improvements are ongoing. This article will explore the journey that breast surgery has undergone and what we can learn from its evolution.

William Halsted (born 1852) was an American surgeon whose contributions have influenced surgical principles to this day. [3] He is considered one of the 'Big Four' founding physicians of John Hopkins Hospital. [4] He pioneered the use of the hospital chart, advocated careful handling of tissue during surgery and stressed the importance of haemostasis. [3-6] His name is also synonymous with the radical mastectomy that he introduced in 1882. [3] At that time attempts at breast surgery had resulted in poor long term results and prognosis. [6,7] This new surgical approach was revolutionary in the treatment of breast cancer. The radical mastectomy was implemented for breast cancer no matter the size of the tumour, type, or the patient's age. [8] It typically involves removal of all breast tissue, axillary lymph nodes and both pectoralis muscles. [6] It often results not only in severe disfigurement of the patient but also weakened arm function and disabling lymphoedema. [9] Whilst revolutionary at the time it was pioneered by Halsted, it was still widely used in the 1970s with a 'one size fits all' approach. [8] That approach is very different to the one taken today. [2,10,11]

While there had been some exploration of modifications to the procedure, such as sparing of the pectoralis muscles, as well as further dissection with removal of the internal mammary nodes, the surgical approach to breast cancer remained relatively static for more than eighty years. [8] Although there are many potential reasons this state of inactivity is surely multifactorial. Feminist authors have claimed that the mastectomy was not altered by male surgeons because of the power and control it gave them; that they had no understanding of the importance of a woman's breast to a woman and treated patients in response to this view. [12] Others have suggested that Halsted was held in such high regard that no one dared alter his procedure, with surgeons 'indoctrinated' into his way of thinking. [12,13] Perhaps it is also that the nature of the disease affected how it was approached, with surgeons hesitant to make changes to a procedure they believed could save the lives of countless women. This seemed to be the case for Halsted himself who suggested, "After all, disability, ever so great, is a matter of very little importance as compared with the life of the patient." [6] It must be acknowledged that in Halsted's time there was no method of grading or staging cancers as there is now, a problem he recognised stating, "the importance of such a classification, if it were to any extent possible, is so evident that it is unnecessary to emphasize it." [7] Had he had such information available to him his approach to individual cases may have varied greatly.

Alterations to the mastectomy were taken cautiously. There were forays into and case reports of the super-radical mastectomy, simple mastectomy and use of radiation therapy, as well as some use of simple excision; however no clear evidence as to the differences was available.

[8] In 1969 the World Health Organisation approved a randomised control trial comparing radical mastectomy to the 'quadrantectomy'. [8] Recruitment began in 1973 of patients staged with T1N0 disease who were aged less than 70 years. The quandrantectomy was combined with complete axillary dissection and postoperative radiotherapy. Early data demonstrated no difference in regards to survival rates, and the similarities in the long term survival rates were confirmed in data released in 2002. [8] In 1971 Fisher et al commenced a randomised trial comparing the radical mastectomy with total mastectomy with or without radiotherapy. [14] Studies such as these heralded the advent of breast conserving surgery and the acknowledgement that routine radical mastectomy may not always be the most appropriate surgical management.

Halsted proposed that although breast cancer begins as a local disease, it spreads in a contiguous manner away from the primary site through the lymphatic system. [6,15] This proposal led to his emphasis on aggressive locoregional treatment to prevent further spread. [6,7,12,15] This principle, however (known as the 'Halsted Theory'), was also critical in introducing the concept of a sentinel node in relation to breast cancer. [15] Research into the sentinel node led to the use of the sentinel node biopsy which has dramatically influenced surgical management and outcomes for patients. One of the first studies demonstrating the benefits of lymphatic mapping for breast cancer was published by Guiliano et al in 1994. [16] Since that time the evidence, understanding and surgical skills in this area have grown rapidly.

Modern day surgery for breast cancer has changed significantly compared to that performed in the 1970s. The combination of breast conserving surgery alongside a sentinel biopsy allows patients to be left with good cosmetic results. [17,18] Oncoplastic techniques such as remodelling mammoplasty are also being utilised to improve cosmetic outcomes without compromising adequate tumour removal. [19,20] There is still however an appropriate place for the mastectomy. [20] Breast conservation is desirable, but needs to be acceptable cosmetically and not result in compromise to local control of the disease or survival benefit. [17,19,20] If local recurrence does occur following breast conservation, then salvage mastectomy is considered the standard approach, with salvage breast-conserving surgery only currently appropriate for consideration in select patients. [21]

Reconstructive breast surgery is an important part of management utilised by surgeons today. It is significant in improving the psychological

morbidity associated with breast cancer surgery, particularly following mastectomy. [2,22] Once again Halsted had an influence in this area of breast surgery. He believed reconstruction was a "violation of the local control of the disease". [10] Although there were a few early attempts at breast reconstruction by the likes of Czerny, Tanzini and Ombredanne, [23-25] the opinion put forward by Halsted and the view that local recurrence may not be detected if reconstruction occurred caused it to be avoided. [2,10] It seems, however, that surgical exploration of reconstructive procedures during this period was considered more than the possibility of breast conservation was. [8,10] This supports the view that surgeons at the time believed the mastectomy was crucial to life saving treatment and it was this belief that prevented progress to other initial surgical approaches. [13]

Following the introduction of the mastectomy in 1882 there were surgeons willing to attempt reconstructions to improve the quality of life of their patients. [2,10,22] In 1963 these efforts were bolstered by the silicone gel breast implant introduced by Cronin and Gerow. [26] In 1971 Snyderman and Guthrie placed an implant under the chest wall immediately following a mastectomy, as opposed to the delayed technique that had been used, and this was then accepted as the new technique. [27] In 1982 Radovan introduced the concept of skin expanders for those with significant skin deficits so that these patients too could be eligible for reconstructive surgery. [28] Following this skin-sparing mastectomies were introduced, with results demonstrating similar rates of local recurrence. [29] There have also been advances with the use of flaps as a method of reconstruction. [2,10] In regards to reconstruction of the nipple-areola complex, tattooing is now commonplace as initially suggested by Becker in 1986. [30] Today a woman who thirty years ago would have been left with almost no chance of reconstruction can have a relatively symmetrical result. Decisions relating to the method of reconstruction depend on many variables, however it can be seen that important progress has been made in this area of breast surgery. [2,10] This can improve patient perceptions towards treatment and significantly improve their quality of life. [2,22]

The evolution of breast cancer surgery demonstrates important principles when evaluating any surgical procedure. No matter what procedure is undertaken, the most appropriate management needs to be carefully considered with clear clinical reasoning and evidence where available. Despite this there are also many elements which need to be considered when deciding what is most suitable, not all of which are clear without a thorough understanding of both the patient being treated and the disease. The disease cannot be treated in isolation but must be regarded in consideration of the patient's wishes, and often in regards to other health issues. This is especially true in oncological surgery. Treatment decisions cannot often be made simply or alone. They are best made by the patient and the surgeon as part of a multidisciplinary team. [2,22] With regard to breast cancer the tumour itself plays a critical role – its type, size, determination of its spread to lymph nodes or metastatic sites, and whether it is hormonally responsive. [2,22] The size of the tumour is crucial in determining operability, especially alongside a consideration of the size of the breast itself. Tumour size, breast size and the location are important when assessing for the likelihood of future local recurrence as well as the impact on cosmetic outcomes. [2,11,17]

For the appropriate management to be undertaken the surgeon must obtain as much information as possible. The patient's family history and potential for a recognisable genetic factor requires thought. [11] Genetics play an increasingly important role in the management of patients with breast cancer. Along with the well-known BRCA1 and BRCA2 mutations, there are other unidentified genes which lead to strong familial associations. [31] Knowledge of these factors impacts on decisions regarding the surgical management of a particular patient as well as other forms of treatment.

Cost and availability of treatment options are also important in the surgical management of breast cancer. Cost is not often seen to impact on the treatment patients receive in Australia, however it can be overlooked, as can the availability of services and travel required to undergo particular surgical options. [2] These factors are much more pronounced in other parts of the world where only the exceptionally wealthy may be eligible for surgery. [32] It is important to consider the impact of a particular surgical treatment on the need for ongoing follow up and the level to which this will be required. [2,11] No matter which surgical approach is taken it is vital that realistic expectations of the prognostic as well as cosmetic results are discussed with each patient prior to surgery.

Surgical excision deals with local, known disease and comes alongside radiotherapy, chemotherapy, hormonal therapy and biological agents where appropriate. [11,22] These other treatment modalities impact on both prognosis and cosmetic results. [2,11,17,18,22] The role of surgery must be considered in relation to these other factors. Management options for breast cancer will continue to expand in coming years as current therapies improve and new ones emerge, requiring ongoing collaboration. [33]

At a multidisciplinary team (MDT) meeting the many stakeholders involved in a patient's treatment come together. [11,22] No matter which path is chosen for each area of management, it is done in consultation with other experts, with each responsible for justifying their position. [33] Communication barriers are broken down and the full clinical picture is able to be understood by all involved. Although there is variation worldwide as to how MDTs are run, it is perceived that they improve clinical decision making, treatment quality and the practice of evidence based medicine. [33] Interestingly, Halsted himself viewed it as important that the surgeon had an intimate awareness of the pathology which he excised, writing

> *"There is a gap between the surgeon and pathologist which can be filled only by the surgeon. The pathologist seldom has the opportunity to see diseased conditions as the surgeon sees them. A tumor on a plate and a tumor in the breast of a patient, how different!"* [7]

Halsted seemed to advocate that the surgeon's interest and understanding of the pathology was more significant than that of the pathologist. The recognition of multi-disciplinary meetings is that all parties have significant "*incentive*" (as Halsted put it), [7] and by working together the gaps between the theatres, the laboratory and the chemotherapy centre can be closed.

The radical mastectomy is now famous for its brutality. [12] Despite its poor reputation today, by bringing it into existence Halsted caused many women's lives to be saved. We should respect those who have gone before us and learn from their work, whilst at the same time be willing to question and improve upon it. We need to guard ourselves from repeating mindlessly that which we have been taught, without seeking to develop it. Much has changed since Halsted boldly stated, "Tumours should never be harpooned, nor should pieces ever be excised from malignant tumors for diagnostic purposes." [7] This may seem strange considering how we now utilise biopsies, although in years to come the flaws in our own thoughts and practices will be exposed.

Halsted was innovative, bringing discoveries to his time, and he will always hold an important role in surgical history. The French philosopher Gaston Bachelard displayed wisdom in saying "the characteristic of scientific progress is our knowing that we *did* not know". It should be added that scientific progress comes through our knowing there is much we still *do* not know, and it is up to us to seek the answers.

Conflict of interest

None declared.

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Legalising medical cannabis in Australia

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Introduction

Cannabis was first used in China around 6,000 years ago and is one of the oldest psychotropic drugs known to man. [1] There are several species of cannabis, the most common are *Cannabis sativa, Cannabis indica* and *Cannabis ruderalis*. [2] The two main products that are derived from cannabis are, hashish – the thick resin of the plant, and marijuana – the dried flowers and leaves of the plant. [1] Cannabis contains over 460 chemicals and 60 cannabinoids (chemicals that activate cannabinoid receptors in the body). [1,2] The major psychotropic constituent of cannabis is known as delta-9-tetrahydrocanabinol (THC); others include cannabinol and cannabidiol (CBD).

Cannabinoids exert their effect throughout the body through binding with specific cannabinoid receptors. There are two types of cannabinoid receptors found in the body: CB_1 and CB_2. Both are G-protein coupled plasma membrane receptors. The CB_1 receptors are mostly found in the central nervous system, whilst CB_2 receptors are mainly associated with immunological cells and lymphoid tissue such as the spleen, tonsils, and thymus. [3,4]

Delta-9-tetrahydrocanabinol (THC) and other cannabinoids are strongly lipophilic and are rapidly distributed around the body. [5] Because of its strong lipophilic nature cannabinoids accumulate in adipose tissue and have a long elimination time of up to 30 days, although the psychoactive effects generally wear off after a few hours. Medical cannabis can be dispensed and taken in a variety of ways including as a herbal cigarette, ingestible forms, or as herbal tea. However, marijuana cigarettes are commonly preferred as they provide higher bioavailability. [5]

Medical marijuana users represent a large range of ages, levels of education attainment, employment statuses, and racial groups. [6] A Californian study examining medical marijuana use showed 76.6% of medical marijuana users use seven grams of marijuana or less per week. Therefore, the majority of medical marijuana users are likely to consume amounts equivalent to mild to moderate recreational cannabis use. [6]

The rescheduling of cannabis in Australia draws strong debate and opinions from both sides of the issue. This article will provide an overview of the most popular arguments for and against the legalisation of cannabis for medicinal purposes.

The legal status of medical marijuana in Australia

Currently cannabis is a Schedule nine drug in all Australian states and territories, placing it in the same category as drugs like heroin and lysergic acid diethylamide (LSD). [7] Legally, drug scheduling in Australia is a state issue, however, all states abide by the federal government's scheduling of cannabis as a Schedule nine drug, as per the Standard for the Uniform Scheduling of Medicines and Poisons. [7,8] The use of a drug which is classified as Schedule nine for recreational or medical purposes is illegal and a criminal offence. Research into cannabis in Australia is highly restricted. [7] Cannabis use is common in Australia with approximately 40% of Australians aged fourteen years or older saying they have used cannabis, and over 300,000 Australians using it daily. A number of Australians are already self-medicating with cannabis for a range of complaints including chronic pain, depression, arthritis, nausea, and weight loss. However, these people risk legal action from authorities, particularly if cultivating their own cannabis. Moreover, if they purchase cannabis from a dealer they also face quality and supply

issues. [9] Proponents of medicinal cannabis envisage a system similar to other drugs of dependence, like opiates, whereby holders of a valid prescription will be able to purchase or access the drug but where recreational use of the drug would still be illegal.

A number of countries have decriminalised cannabis for medical purposes such as the Netherlands, Israel, eighteen states in the United States of America (USA), Canada and Spain. [10] However, the drugs known as Dronabinol (containing just THC), Nabilone (containing a synthetic analogue of THC) and Nabiximols (a spray containing CBD and THC) are available as Schedule eight drugs throughout Australia. [7] Schedule eight drugs are drugs which have a high likelihood for abuse and dependence and require regulation in their distribution and possession. [7,8] However, some claim that these preparations lack many of the cannabinoids found in natural cannabis plants and this leads to different physiological and therapeutic effects compared to natural cannabis. [4] Public support in Australia for medical cannabis is very high with a survey finding 69% of the public supporting the use of medical cannabis and 75% supporting more research into the medical potential of the drug. [11]

Arguments for legalisation

Pain relief

Marijuana has potent analgesic properties which can be used in pain relief for a variety of conditions that can cause intense pain, such as cancer pain and acquired immunodeficiency syndrome (AIDS). Marijuana may even provide superior pain relief when compared to opiates and opioids. A parallel study in the United Kingdom (UK) compared the use of a THC and CBD extract, a THC only extract, and a placebo in the treatment of cancer pain. It found that a THC:CBD mixture (such as that found naturally in the cannabis plant) is efficacious for the relief of advanced cancer pain that is not adequately controlled by opiates alone. [4] Therefore, the legalisation of medical cannabis could relieve pain and improve the quality of life for severely ill patients suffering from a range of painful conditions.

Appetite stimulation

It has been proven in animal studies that THC can have a stimulating effect on appetite and lead to an increase in food intake. [2,5,12,13] There are a large number of clinical applications for THC for appetite stimulating purposes. Conditions which can cause cachexia (uncontrolled wasting) such as HIV/AIDS, cancer, multiple sclerosis

(MS), could be treated with THC to stimulate the patient's appetite, increase food uptake, restore weight, and improve the strength and wellbeing of the patient. [2,13] Human trials in the 1980s which involved healthy control subjects inhaling cannabis found that the cannabis caused an increase caloric intake of 40%. [14] The legalisation of cannabis for medical purposes could help improve both health outcomes and the quality of life in patients suffering from a range of conditions.

Anti-emetic

In Canada and the USA, dronabinol and nabilone have been used in the treatment of chemotherapy induced nausea and vomiting since the 1980s. [15] A systematic literature review found that cannabinoids were more effective than established anti-emetic drugs in its treatment. [16] By reducing or eliminating the often debilitating and painful symptoms of chemotherapy induced nausea and vomiting, medical cannabis is hoped to improve the quality of life for the patient and their family. A reduction in the vomiting and pain associated with chemotherapy may also cause an increase in adherence to chemotherapy by cancer patients and result in better patient outcomes. [2,13] Therefore, the rescheduling of cannabis could prove as a highly effective anti-emetic for cancer patients and could even improve their prognosis by encouraging adherence to chemotherapy.

Neurological conditions

Cannabis may also be used to lessen or alleviate an entire range of symptoms associated with MS and other neurological conditions. A Canadian randomised, placebo-controlled trial investigating the use of smoked cannabis for MS-related muscle spasticity found that cannabis was superior to the placebo in reducing pain and spasticity. [17] Another trial conducted in Canada on the use of smoked cannabis for chronic neuropathic pain found that an inhalation of the cannabis formulation prepared for the trial three times daily for five days reduced pain intensity, improved the quality of sleep, and had minimal adverse effects. [18] The legalisation of medical cannabis could therefore make a significant difference to the lives of the thousands of Australians suffering MS and many other neurological conditions.

Safety and overdosing

Cannabis may also serve as an incredibly safe alternative to groups of medications prescribed for pain, such as opiates. The CB_1 cannabinoid receptors are the main receptors responsible for the analgesic effects of cannabis and are located in the brain. However, they are in very low numbers in the regions of the brain stem co-ordinating cardiovascular and respiratory control. [2,19] This means it is essentially impossible to overdose from cannabis. [5] However, opioid receptors are located in this brain stem region hence signifying that opioids can interfere with cardiovascular and respiratory functions and lead to death. [19,20] Prescription opioid deaths are a small but concerning issue throughout developed nations. For example, in 2005 there were over 1,000 deaths related to prescribed oxycodone in the US. [20] Medical marijuana may offer a safer alternative form of pain relief as it removes the risk of accidental overdose which can lead to death.

Arguments against legalisation

Cannabis use and psychiatric disorders

A longstanding argument against the medical use of cannabis has been that exposure to cannabis can lead to the development of psychiatric disorders, namely schizophrenia. A Scottish systematic review of eleven studies investigating the link between marijuana use and schizophrenia supported this view and found that cannabis use did appear to increase the risk of schizophrenia. [21] Another study has also shown that there is an association between heavy cannabis use and depression. [22] Further effects of cannabis induced psychosis can include self-harming and self-mutilating behaviours. [23,24] The relationship between cannabis use and mental health issues appears to be dose-related with higher amounts of marijuana use related to more severe psychiatric complications. [21,22] Some say it would be unethical to prescribe a patient cannabis when there is a risk of the patient developing mental illness and potentially harming themselves or others. Particularly, when there are other drugs available without such adverse effects on mental health and stability.

Public safety

With the legalisation of medicinal cannabis come clear public safety concerns, particularly in the areas of vehicle and pedestrian safety. Cannabis affects the brain and can cause feelings of disorientation, altered visual perception, hallucinations, sleepiness, and poorer psychomotor control. [5,19] A study conducted in California found that on a particular evening, 8.5% of motorists had THC in their system and that holders of a medical cannabis permit were significantly more likely to test positive to THC than those who did not hold a permit. [25] It has also been shown that drivers using cannabis had about three to seven times the risk of being in a motor car collision than drivers who were not using cannabis. [26] However, it is interesting to note that those driving under the influence of alcohol were at a higher risk of having a collision than those using cannabis. [27] Also interesting is the fact that after medical marijuana programs were instituted in the US, traffic fatalities decreased nine percent across the sixteen states which had programs at the time of the study; this is believed to be due to a substitution of alcohol with marijuana. [27,28] Pedestrians and cyclists who are prescribed cannabis are also at higher risks of being injured in a collision. In terms of non-vehicular injuries, an American study showed cannabis use was associated with an increased risk of injuries from causes such as falls, lacerations, and burns. [29] Hence the legalisation of medical cannabis not only poses a risk to the personal safety of the patient but also to the physical safety of the wider community.

Drug diversion

Given the popularity of cannabis as a recreational drug, there is always the risk of wide scale drug diversion occurring–that is people without a prescription for cannabis gaining access to the drug. This can happen in a number of ways like a patient sharing their medication with others or the patient selling their medication. In America diversion of medical marijuana is an increasing issue, particularly amongst adolescents. A study in the state of Colorado in the USA found that out of a group of 164 adolescents at a substance abuse treatment facility, 74% had used someone else's medical marijuana, with the mean number of times the adolescents had used someone else's medical marijuana being over 50. [30] Illicit use of cannabis for non-medical purposes exposes people to the damaging physical, mental and social impacts of drug use. There are clear questions surrounding how this would be prevented and how young adults especially could be prevented from accessing cannabis due to diversion. It must be asked whether it is ethically responsible to reschedule marijuana given that such a large number of other people, particularly adolescents, will have access to someone else's medical cannabis.

Addictiveness and dependence

The legalisation of cannabis as a medication has the potential to cause patients to develop an addiction to the drug and possible dependence. Cannabis dependence is a recognised psychiatric disorder and it is estimated that over one in ten people who try marijuana will become addicted to it at some point. [31] Although dependence to marijuana may be lower than other drugs like, heroin, cocaine and alcohol, users can still face withdraw symptoms including sleep difficulty, cravings, sweating and irritability. [5,32] With the potential of people becoming addicted to medical cannabis and with scarring consequences for their personal life some say it is ethically questionable to subject people to it in the first place.

Availability of cannabinoid and synthetic cannabinoid drugs

Those opposed to cannabis being rescheduled for medical purposes claim that the availability of cannabinoid and synthetic cannabinoid

drugs already in Australia namely, Dronabinol, Nabilone and Nabiximols, makes legalising medical cannabis unnecessary. They state that these drugs contain many of the same compounds as cannabis and can be used for treating many of the same conditions. [13] For example, Dronabinol has been shown to be effective in relieving patients suffering chronic pain which is not fully relieved by opiates. [33] Therefore, the cannabinoid medications which are already available in Australia may provide many of the same therapeutic benefits offered by cannabis, and as such rescheduling cannabis would be unnecessary.

Carcinogenicity

Whether marijuana smoke causes cancer, in particular lung cancer, is a subject of much debate and research itself. It is well established that tobacco smoke is carcinogenic and deeply damaging to overall health. [34] With marijuana containing many of the same carcinogens as tobacco, and often being in cigarette form, it is not unreasonable to expect similarly adverse results with cannabis use. [5,35] However, a case-control study by Hashibe et al. [36] found that there was not a strong relationship between marijuana use, even in heavy amounts, and the incidence of oesophageal, pharyngeal, laryngeal, and lung cancer. Some evidence exists, showing that cannabinoids may in fact kill some cancers such as gliomas, lymphomas, lung cancer and leukemia. [37-39] Despite evidence that marijuana smoke contains mutagenic and carcinogenic chemicals, epidemiologically this was not confirmed to be the case. [35,36] Overall the carcinogenic or cancer-fighting properties of marijuana remain unclear and contradictory. More long-term, large population research should be conducted so that the seemingly contradictory nature of the drug can be better understood. [36]

Recommendation

Cannabis offers exciting possibilities for patients afflicted by cancer, HIV/AIDS, MS, chronic pain and other debilitating conditions. Although medical marijuana programs face several obstacles, the benefits offered by medical marijuana and the positive impact this drug could have on the lives of thousands of patients and their families make a strong case for its consideration. The potential drawbacks can be minimised or even overcome through a number of measures, including: the close medical supervision of patients (e.g., proper patient education and monitoring), the creation of appropriate infrastructure (e.g., medical marijuana dispensaries, as seen in California) and the creation of laws and policies that are not only supportive of medical marijuana patients but will also, minimise the risk the drug poses to the public (e.g., strict penalties for medical marijuana diversion).

Conflict of interest

None declared.

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Fiction and psychiatry: The tale of a forgotten teacher

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"Wherever the art of medicine is loved, there is also a love of humanity." -Hippocrates

Reading this declaration today, conjures an unsettling, or almost unpleasant feeling that this once foundational concept may today be lost in time. A 'love for humanity', whilst still lingering in the minds of some clinicians has been largely side-lined by science, research, evidence based practice, being mindful of patient's rights, family criticisms and practicing medicine with caution against being sued or criticised ourselves. We may benefit to keep in mind the words of American, philosopher Will Durant, "Every science begins as philosophy and ends as art."

Ironically, it seems that science may provide answers to the apparent diminution of humanity in medicine. A recent editorial advocated that empathy in medicine may have a neurobiological basis and therefore can be up-regulated through specific neurobiological correlated education methods, in order to enhance professionalism and compassion.[1,2] Suggestions such as these reflect society's growing dependence, or perhaps near enslavement to science which may soon become a surrogate for what were once regarded as inextricable, innate, features of our humanity – empathy and wisdom.

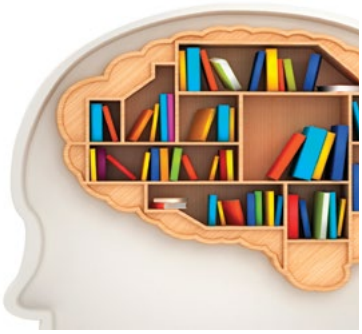
Beveridge reminds us that, "Doctors need a deeper understanding of their patients that takes account of emotional and existential aspects."[3] Literature offers us a multitude of human experiences that may serve to deepen our appreciation of the breadth of human consciousness. As T.S. Eliot stated, "We read many books, because we cannot know enough people."[3]

Psychiatry is one field of medicine which demands a strong level of empathy and a sophisticated level of interpersonal communication. Psychiatry studies the human mind with its complexities of emotions, behaviours, motives, experiences and reactions. Crawford describes the existence of a 'synergism' between literature and psychiatry as they both focus on the human mind from two separate paradigms: first, a scientific, biomedical framework of medicine; second, an artistic, creative medium of fiction. He questions, despite this congruence, why does literature still 'remain the poor relation of the medical textbook?'[4] The concept of two paradigms, or a dualisms of brain and mind is explored further by Australian philosopher David Chalmers who describes how these two entities are different and how understanding each one requires a unique method.[5]

It is at this junction, between clinical psychiatry and fictional literature that our journey begins. This essay will explore some of the reasons for why we, as students and health professionals should and should not engage in fictional reading. We will then delve into some literary examples that provide insight into mental illness.

Benefits of fiction

Reading fiction may allow us to better connect with individuals such as our patients emotionally by first connecting with fictional characters. Evans proposes that when we read for enjoyment, *"Our defences are down – and we hide nothing from the great characters of fiction."*[6] He contrasts this to a doctor-patient interaction where doctors, *"do [their] best to hide everything beneath the white coat, or the avuncular bedside manner."* Over many years, all that is left is a professional, clinical interaction at the cost of a personal connection with the patient. He reminds us that, *"It is at this point where art and medicine collide, that doctors can re-attach themselves to the human race and re-feel those emotions which motivate or terrify our patients."*[6]



Psychiatry tends to place a greater emphasis on thought form when making diagnoses, whilst the patients are more concerned with thought content, even though a doctor may at times miss the subtleties in form too. Literature can make us more aware of the importance of the content to the individual and connect more closely with the patient's experience. Sims illustrates this:

"The patient is only concerned with the content, 'that I am pursued by ten thousand hockey sticks.' The doctor is concerned with both form and content, […] in this case a false belief of being pursued. As far as the form is concerned the hockey sticks are irrelevant. The patient finds the doctor's interest in form unintelligible and a distraction from what he regards as important. […] The nature of the content is irrelevant to the diagnosis."[7]

The analysis of thought form leads us to a clinical diagnosis which justifies clinical interest in form over content; thought process over a patient's narrative. Crawford hypothesises that with the increasing biomedical dominance in psychiatry, there is bound to be further marginalisation of content. He argues that in fiction, the content, which encompasses all human experiences, emotional responses and behaviours, is more valuable and effective in conveying an understanding about the narrative than the form.[4]

Shortcomings of fiction

Not everyone values literature in the context of medical progress – Wassersug proclaimed that, "Real medical progress has not been made by humanitarians but by doctors equipped with microscopes, scalpels, dyes [and] catheters, […] similarly psychiatry should be seen as a branch of the natural sciences."[3] He argues that literature has nothing to offer to psychiatry, a field which should be led by advances in neurosciences, not narrative.

Reading has been described as a 'selfish' activity that can expand individual intellect but cannot instil a spirit of altruism or increased sensitivity towards others.[3] The physician Raymond Tallis illustrates how reading may in fact make us less empathetic; he quotes Tolstoy's tale of an aristocratic woman weeping over a theatrical tragedy, while outside a real tragedy eventuates as her faithful coachman freezes to death. This anecdote highlights the ability of the arts to delude the woman, to believe herself to be sensitive, when in fact she is actually being inconsiderate.[3] Some arguments against reading fiction may be valid. However, they are not sufficient to completely discredit the opportunity fiction provides us to expand our sense of enlightenment, self-development and inspiration in a way that a factual textbook simply cannot.

Fiction and mental illness

Literature is an instrument to present facets of mental illness that may not be captured through textbooks, lectures or case presentations.

Oyebode suggests that fictional narrative achieves its aims by magnifying or exaggerating specific aspects of characters such as their mannerisms, behaviour or speech to make them stand out to the reader. Oyebode analyses Patrick McGrath's Asylum to illustrate how delusional jealousy may be the result of multiple trivial everyday occurrences:

"Driven by the morbid processes to suppose that his wife was betraying him with another man, he had reasoned first, that they must have ways of signalling their arrangements, and second, that their activities must leave traces. He had then manufactured evidence of such signals and traces from incidents as banal as her opening a window as a motorbike was going past in the street below, and from phenomena as insignificant as a crease in a pillow or a stain on a skirt."[8]

Oyebode presents a detailed, focussed magnification on the protagonist's paranoid, obsessive thoughts about everyday occurrences. This allows the reader unrestricted access into the thoughts that occupy a person's mind suffering with delusional jealousy.

Oyebode provides a glimpse into nihilistic thoughts through McGrath's *Spider:*

"I was contaminated by it, it shrivelled me, it killed something inside me, made me a ghost, a dead thing, in short it turned me bad […] I wonder…what they will find when they cut me open (if I'm not dead)? An anatomical monstrosity surely."[8]

The emotive and dark imagery in this writing serves to illuminate the depth of nihilism; the torment the protagonist faces at the mercy of his own mind. Once again, the account provides important insight into a paradigm of thought that may otherwise be foreign to an external observer.

Jenny Diski describes the experience of depression beautifully in *Nothing Natural:*

"Here it was again. Unmistakeably it. […] A physical pain in her diaphragm, a weight as if she had been filled with lead, the absurd difficulty of doing anything - automatic actions having to be thought out to be achieved: how do you get across the room, make the legs move, keep breathing, think carefully about it all. […] The unreasonable difficulty of everything made more unreasonable, more difficult knowing that nothing physical was wrong. […] Depression was an excess of reality: intolerable and unliveable."[4]

This detailed deconstruction of depression exposes the destructive power of depression to render a person physically powerless whilst they are mentally completely aware of what is happening to them. Literature forms a bridge between the internal world of our patients and our global comprehension of their condition. This bridge elevates us from helpless bystanders to active and effective treating practitioners.

Sometimes the words of fictional characters may attack the reader directly, encouraging the reader to engage in self-reflection. The protagonist, from Kristin Duisberg's *The Good Patient,* expresses that mental health practitioners:

"have chosen their profession to deny a terrifying truth other doctors accept – there are ills for which there is no cure."[4]

At first glance this idea seems completely bizarre, as no psychiatrist believes they can cure all psychiatric conditions. However, it is hard to completely dismiss it without the thought lingering on in our subconscious. This attack stimulates some introspection to determine whether there may be any truth behind it at all. The words of this fictional character have the power to leap off the pages, and into our subconscious to question our role and limitations when treating patients with mental illness.

Literature tries to 'de-pathologise' mental illness as evidenced by Sally Vickers in *The Other Side of You:*

"We are most of us badly cracked and afraid that if we do not guard them with our lives the cracks will show, and will show us up, which is why we are all more or less in a state of vigilance against one another."

By addressing this 'cracked' nature inherent in all of us, the author indirectly places all of us on a spectrum of mental illness. She implies, the only difference between mentally healthy and ill is where we stand on this spectrum. Concepts such as this break down the differences between 'normal' and 'mentally ill' and help liberate us from our own inbuilt stigmas against mental illness.

An extensive list of texts and their relation to mental illness can be found at www.madnessandliterature.org

Commentary

Literature, good TV and theatre for that matter, may not completely depict psychiatric psychosis or other psychiatric conditions in their entirety and complexity. They do however give us a glimpse into the differences between internalising (major depression, generalised anxiety and panic disorders, phobias) and externalising (alcohol and drug dependence, antisocial personality and conduct disorders) disorders.

We find ourselves in an age where the growth of information, triumphs of science and expansion of technology appears to be propelling us into a biomedical dominated practice of medicine. The question that we must ask ourselves is whether this scientific dominance is encroaching on our capacity for empathy, understanding and appreciation? Fictional literature may provide us with an opportunity to re-connect to our humanity in a way that no other medium can. Literature may not make us better diagnosticians, or change the value system of our profession, but it will make us question ourselves, our thoughts, and our perception of others. This new level of reflection and understanding can result in a more wholesome interaction with patients which will strengthen the therapeutic alliance between patient and doctor.

The study of humanities should not take priority over crucial clinical elements, but it can be used as an adjunct to clinical education. There is evidence to suggest benefit of reading already, and a number of medical schools have implemented medical humanity subjects and faculties because of their appreciation of its inherent value.[9-11] However, reading is something that is not restricted to the classroom; it cannot be tamed by our teachers and it has a timeless ability to touch us if we let it. Alexandra Trenfor writes, "The best teachers are those who show you where to look but don't tell you what to see," and fiction is like this teacher – it provides us with a narrative, but leaves its meaning and essence for us to discover ourselves.

Conflict of interest

None declared.

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Emergency medicine in Australian medical student education

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"The best way to predict the future is to invent it." Alan Kay

Introduction

As the coalface of Australian healthcare, Emergency Medicine (EM) faces the growing healthcare challenges of the wider community. Today, these challenges form a unique 'triple whammy' – overseeing the implementation of the National Emergency Access Target (NEAT) or "4-hr rule", in an effort to manage access block and emergency department overcrowding as a result of the increased care needs of an ageing population, whilst at the same time with limited resources attempting to maintain the quality of education and training of a burgeoning junior medical workforce. [1,2]

Amidst this conundrum, medical student EM education may sometimes be left in the shadows. [3,4] The unique arena of the emergency department with its volume, breadth and variety of undifferentiated patient cases not only provides countless learning opportunities for medical students but also allows them to contribute to healthcare teams in practical and meaningful ways. This ranges from assisting in initial assessments, to performing indicated procedures, to formulating discharges, and even research involvement. [5,6] All of which are useful and valuable skills favoured upon in a junior medical doctor and reduces the workload of the supervising team. [7-9] While some may argue that the general wards offer similar opportunities, the increasing attempts in improving efficiency and subspecialising medicine have led to the bulk of diagnostic and therapeutic interventions to be conducted in the emergency departments prior to acceptance by inpatient units. [4]

Students themselves find EM rotations extremely valuable, with many practical benefits for their future medical careers. [10] However, the already hectic and stressful EM work environment, coupled with enhanced time pressures from NEAT, increasing numbers of interns needing to complete an ED term, and the significant teaching and supervision requirements within EM departments may prove to be hurdles that limit the chances for medical students' education. [11]

Thus, it may be prudent to re-examine this issue of our workforce challenges and to re-assess medical student education.

1. Could added investment in extension and evaluation of EM to medical students pique their interest in a future EM career?
2. Would an increased focus on EM teaching better equip and innovate Australia's future healthcare workforce?

Why is EM important in medical student education?

As a population-based specialty, EM education offers medical students a glimpse into the domain of public health. Patients present with illnesses and injuries that have high population prevalence, and presentations vary even across times of the day. Students are therefore exposed to a dynamic socioeconomic, cultural and demographic case mix. This serves to broaden not only the variety in conditions that students would see within an EM rotation, but also widens their perspectives on pertinent issues affecting different age groups in the

Australian healthcare setting.

EM also provides an opportunity to learn about pre-hospital care, including co-ordinating ambulance and paramedic transfer services, retrieval, wilderness and disaster medicine. Students encounter clinical scenarios they would not otherwise see such as occupational and environmental health, toxicology and trauma, and are also exposed to accident and injury surveillance, treatment and prevention.

EM has unique content areas that form the foundation of medical student training. In fact, EM exposure is seen as a form of clinical training assurance and a measured criterion for both students and junior doctors to be work-ready, and is considered essential and highly valuable as a core intern term in all states around Australia. [7]

With each undifferentiated presentation, students are encouraged to complete a focused history and examination, consider emergency interventions and prioritise differential diagnoses, rather than needing to pinpoint a correct diagnosis in a second. They then formulate streamlined investigation and management plans, and have opportunities to perform basic procedures which form part of the initial evaluation of many patients. Students can also receive positive feedback and critique from clinicians on their performance, and even observe and learn from their more senior colleagues in managing acutely ill patients. [4]

There are other unique benefits of students training in the ED environment. With the rollout of NEAT, clinicians may be increasingly pressured to make time-critical evaluations and decisions. Students would therefore not only be able to observe time and cost effective patient assessment strategies but also hone problem solving and task prioritisation skills. [12] The acute management of common ED presentations would be better appreciated as fewer patients stay in the ED for hours or days and are transferred to the wards within four hours. Furthermore, a minimum of 40% and up to 73.3% of patients within the ED are available for directed-learning purposed interaction with student doctors – a significantly higher percentage than inpatient wards. [4,13]

Many EDs now also contain short stay units (SSU) where patients requiring short admissions or periods of observation are managed. A

multidisciplinary healthcare team is often involved in the care of these patients, and students are able to work with the team and are involved in allied health discussions and discharge planning meetings.

How can students learn more?

Access

Medical students are usually not rostered on overnight shifts due to a lack of senior medical staff and thus inadequate supervision. A 24-hour rostering of students may be one way to combat the need for more placement opportunities, provided it does not overload junior medical staff. Elective night shits have already been occurring though there is no current data evaluating medical students' learning during those specific shifts. Nonetheless, there would be benefit in providing observational exposure to a different case-mix of patients, especially in resuscitation situations, where students can play a more hands-on role during night shifts.

E-learning

Simulation skills laboratories have been a proven tool in improving theoretical knowledge and procedural skills for medical students, especially in deteriorating patient or acute resuscitation scenarios. [14] These courses, along with other electronic resources can also be utilised for on or off-site learning. More traditional trauma training courses and more novel methods such as cadaver based simulation course for advanced emergency procedures have also proved useful in equipping medical students with basic and advanced procedural skills. [15]

Decision supports

Competency-based training including the use of logbooks and clinical pathways has been shown to improve quality of care in some areas of medicine. [16-18] Logbooks are currently used at various specialty training colleges including ACEM, and adoption for EM education can assist students to measure their abilities against a minimum standard. Medical diagnosis or treatment protocols or checklists can also guide students in developing a systematic approach to evaluating and treating various conditions.

How can students contribute more?

Previous research has shown the potential benefit that engaging medical students as paid assistants of the healthcare team can have on performance efficacy and workflow. Pilot projects have been tested in Germany and the USA. [8,9]

If introduced, a similar system within the EM departments where medical students assist in triaging patients, undertake basic procedures and complete preliminary paperwork alongside a nurse or rapid assessment clinician may expedite care and reduce waiting times for patients. They could also aid in collating relevant medical information from GPs, specialists, residential care facilities and families. This would ease the paperwork burden for clinicians, improve efficacy of clinician-patient contact time and at the same time provide learning opportunities for students whilst collecting and synthesising information.

Medical students can also play an important role in academic aspects of EM. It is sometimes difficult for clinicians to allocate specific time for research whilst balancing patient care; thus students can assist in identification and recruitment of subjects, drafting of protocols and briefing of staff members on ongoing projects.

Where to from here?

The immediate challenges EM departments face should not deter EM clinicians' involvement in training medical students for the future. [11] Rather, a collaborative effort with students to enhance EM learning will give future doctors a skillset applicable in any emergency scenario, regardless of specialty area.

As such, students' feedback on EM rotations and learning techniques should be considered when planning EM curricula. Allocation of dedicated teaching time and educators along with adequate funding for implementation of various initiatives such as e-learning and simulation courses should also be made available for use.

Further research evaluating the current state of EM medical student education nationwide is crucial to identify key areas for improvement. Pilot projects testing novel ways such as those listed above to allow students to contribute to EM departments will also be beneficial to further evaluate innovative learning techniques.

Despite the added cost and effort required, EM training has proven invaluable for medical students and remains an essential part of their training. It is therefore highly recommended that EM continues to maintain a strong presence in medical students' curriculum. [5]

Conflict of interest

None declared.

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Perhaps the only ECG text you need….

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Jayasinghe, S. Rohan. *ECG Workbook*, Australia: Elsevier; 2012.

RRP: $59.95

This is an Elsevier supported book review

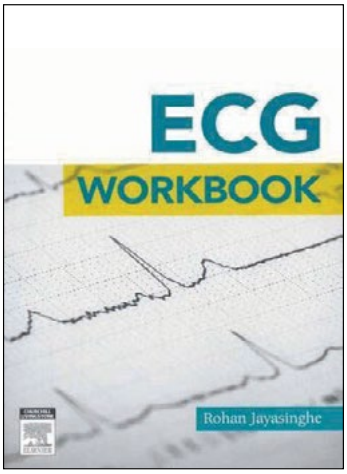
Like tools are to a plumber, correct ECG interpretations are to a doctor. ECGs are the basis of diagnosis for many of the patients that walk through our hospital doors. Consider this: how many patients do you see that don't have an ECG tucked into their notes? And how often have you looked at an ECG and quietly thought to yourself, "what on earth is going on?" before sheepishly praying that the consultant doesn't ask you to interpret it? Mastering an ECG is the foundation of being a doctor, an essential skill that you will not be able to shy away from. So in a quest to find a tool that would ease my ECG fears, I stumbled across this clever little book.

Jayasinghe takes both a logical and systematic approach in this text as he emphasizes the "importance of treating a patient and not an ECG". Readers are provided with real life case studies and guided through a stepwise process to interpret an ECG. This provides an opportunity to not only practice this new skill set but also to formulate a clinical diagnosis and decide on appropriate and optimal management.

The workbook is divided into three convenient user-friendly sections.

Section 1 takes readers on a journey through the fundamentals of ECGs. Essential knowledge on cardiac conduction physiology is revisited, before explaining the derivation of the modern electrocardiogram by the Nobel prize-winning Dutch physician William Eithoven. Difficult concepts (for example, the accurate determination of the cardiac axis) are explained using both the two and three lead method. This is discussed before using a difficult yet more accurate methodical explanation of its relation to a hexa-axial reference system. The importance of correct limb placement is clarified before the author dives into providing the reader with six practical rules that should be applied when 'eyeballing' any ECG. This framework then provides an organized line of attack when attempting to read an ECG. Overall Section 1 studies the 'normal' ECG and highlights life-threatening ECG changes that require urgent therapeutic intervention.

Section 2 explores ECG based diagnosis through interpreting pathological ECGs, highlighting areas of study such as abnormalities in the P wave, PR segment, QRS complex, Q wave, R wave, S wave and ST segments. This section then focuses on STEMI associated ECG changes. The author should be commended for including pathologies with mixed ECG changes which are commonly seen in clinical settings such as pulmonary embolism, subarachnoid haemorrhage, takotsubo cardiomyopathy, hypokalaemia and hyperkalaemia before drawing the reader's attention to drug induced ECG changes.



Everyone knows that practice makes perfect and that the key to mastering any new skill set is practice. The final section of this innovative book is clearly set out in workbook format containing a series of ECG tracings linked to a clinical scenario. A fill in worksheet guides the reader to interpret the ECG using the strategic framework taught in Section 1.

Many texts that attempt to help the reader master the art of ECG interpretation lack this crucial worksheet approach, which facilitates repetitive learning and ultimately allows the student to master the ability to interpret ECGs in the clinical context. Each case is followed by the answer, which has been carefully set out in the same systematic framework taught throughout the text. The author has clearly placed much effort into ensuring that the reader understands the importance of using a stepwise approach when faced with this somewhat daunting task. Additionally, the author endeavours to engage readers to teach them to stratify the significance of the ECG findings based on clinical relevance and urgency. This is a refreshing approach from a medical textbook.

Self assessment enables the reader to build confidence and precision, to gauge their competence and to hone weaknesses. Key concepts can be revisited and mastered as they work their way through this glorious all-in-one paperback.

This short but sweet text provides a comprehensive and systematic approach to learning ECG interpretation whilst ensuring relevancy to real life scenarios. The only criticism I have of this clever little lifesaver, which is small enough to effortlessly carry around hospital, is that it should be available in hard-back! All things considered, the author, an interventional cardiologist, should be applauded as he has succeeded in providing readers with the perfect balance of mastering the art of ECG interpretation whilst being able to apply it to diagnostic situations without getting lost in the detail.

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