



Australian Medical Student Journal

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Feature

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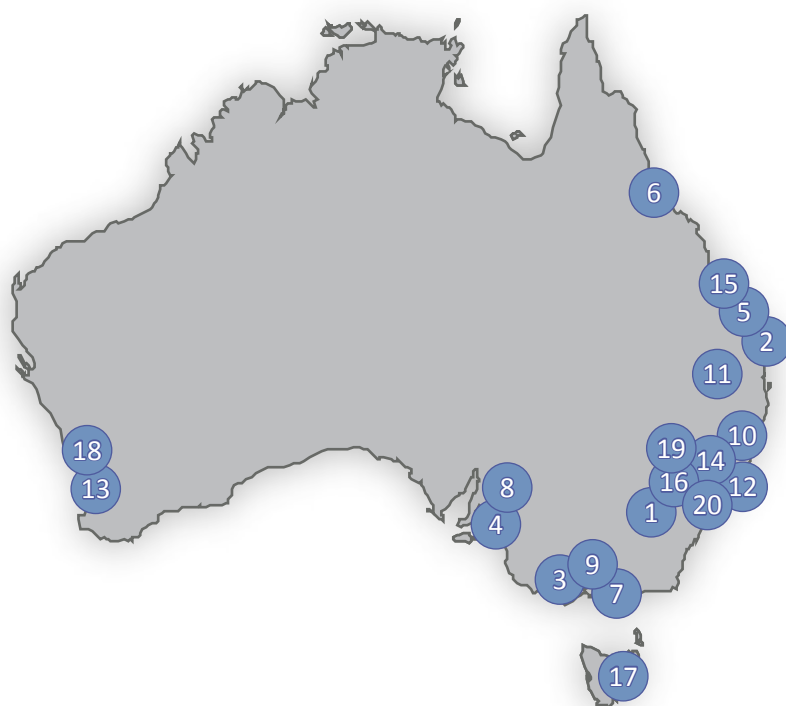
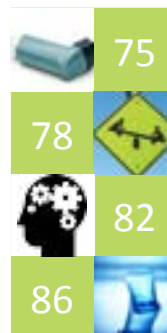
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Editor's welcome: The renaissance men and women of the future

Jessica Chan

Editor-in-Chief, AMSJ

Welcome to a Volume 6 Issue 2 of the Australian Medical Student Journal (AMSJ)! I am proud to showcase the work of talented medical students and to keep our readers apprised of the latest medical research and news. The following review articles, editorials, feature articles, case reports and original research demonstrate the wide variety of medical student interests and expertise.

Medicine is both a science and an art. Medical students are required to be Renaissance men and women, mastering not only the vast expanse of medical knowledge, but also the ability to listen to, empathise with and comfort our patients. As Stephanie Chapple explores in her feature article Medical humanities and narrative medicine, while the technical and scientific aspects of medicine are important, equally so is the development of a good approach to, and understanding of, the patient experience in a way that affirms fundamental respect for their personhood. This sympathy should also extend to our colleagues, particularly in relation to the problem of substance abuse among medical students, as discussed in the feature article by Lewis Fry. Truly, medicine is the art of applying scientific knowledge to provide healing and solace to our fellow human beings.

In addition, the modern practitioner must be acutely aware of the moral dimensions of healthcare, which are increasingly complex as our scientific capabilities grow. As such, I am pleased to introduce in this issue a new section of the AMSJ: 'Debate', where a bioethical topic is disputed by two experts. For the inaugural Debate, Dr Hunt and Prof MacLeod - both highly experienced palliative care staff specialists - argue for and against

the legalisation of voluntary euthanasia.

Other exciting developments in the AMSJ include the revival of the AMSJ Blog, which I encourage everyone to read and comment. AMSJ has also begun collaboration with the Australasian Surgical Students' Conference, and I am delighted to publish the winning abstracts of their 2015 Research Competition.

As future medical practitioners, changes to the medical workforce are extremely relevant to us. The guest article from our partner, the Australian Medical Students' Association (AMSA), discusses the new Curtin University medical school, and why AMSA believes this would only exacerbate, not alleviate, medical workforce problems.

On a more individual level, many of us have pondered our future career options. Read Adrian Lee's editorial about the expanding role of pathology in medicine, and how this affects its desirability as a career. Meanwhile, Neeranjali and Swaranjali Jain discuss in their editorial how global health benefits future doctors not only abroad, but also here at home in Australia. Alternatively, turn the page to Aditya Tedjaseputra's feature article on becoming a haematologist, and how the Australian system differs from that of the United Kingdom. As the practitioners of tomorrow, it is imperative that medical students start being informed of career pathways today.

The AMSJ is brought to you by huge teams of dedicated volunteers from every Australian medical school, who sacrifice hefty amounts of their time and attention. Especial thanks to David Jakabek, my Deputy Editor-in-Chief, and my team of Associate Editors, who ensured the following articles are of the highest standard. Thanks also to Matt Megens and



Jesse Ende the Senior Proof Readers, and their team, who ran the tightest proof reading ship in AMSJ history, and to Jane Guan and Noel Chia the Print Publication Officers, who swiftly laid out this entire issue with cheer and aplomb.

During the production of this issue, I had the privilege of working with two Internal Directors. Thanks to Mr Christopher Foerster, the outgoing Internal Director, your patience and vision for the AMSJ was inspiring. Thank you to Ms Karen Du, our incoming Internal Director, for your hard work. Along with Ms Grace Yeung, the External Director, I welcome you to the AMSJ family, and I am sure AMSJ will continue to thrive under your leadership. Finally, I would like to thank our readers, authors, peer reviewers and sponsors who make AMSJ possible.

On behalf of everyone at the AMSJ, I hope this issue leaves you captivated, enlightened and thoughtful, long after you have put down the journal!

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Executive statement

Grace Yeung

External Executive Director, AMSJ

Karen Du

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THE AUSTRALIAN MEDICAL STUDENT JOURNAL was the brain-child of a group of UNSW medical students in 2010.

BORN OUT OF A PASSION TO RAISE UP THE NEXT GENERATION OF MEDICAL RESEARCHERS AND TO CHALLENGE THE FRONTIERS OF MEDICINE AND SCIENCE, OUR JOURNAL HAS SINCE GROWN INTO A LEADING NATIONWIDE STUDENT PUBLICATION WITH THOUSANDS OF FOLLOWERS.

This year marks the 5th anniversary of this landmark journal. With it, we also embrace many exciting milestones and developments.

In January this year, our Facebook page following skyrocketed to 7,000 members, reflecting the continued expansion of our national readership. We have also revamped our e-newsletter, creating a vibrant new email publication with a distinctive focus on the wonders of the science behind medicine.

Our regular glossy publications, sent to all major medical campuses in Australia, are as vibrant as ever, with this issue showcasing winning entries from winners of the Australasian Students' Surgical Conference (ASSC). Our hardworking Editor-in-Chief, Ms. Jessica Chan, has also brought into being an exciting new section of our magazine, 'Debate'. In it, specialists present the case for and against hot-button medical ethico-legal issues *du jour*.

In addition to the exciting new changes in our publications, we also warmly welcome new additions to our staff team, in particular Ms. Karen Du, who has taken the helm in

the Internal Department, succeeding Mr Chris Foerster as the new Internal Executive Director. With her demonstrated passion for medical research and rich editorial experience both here at home in Australia, as well as in the United States, we look forward to seeing her contributions with us in the journal.

As Mr. Chris Foerster moves on from his role in the AMSJ staff body to the Advisory Board and pursues his career interests both in Australia and overseas, I would also like to sincerely thank him on behalf of the staff body of the AMSJ for his incredible commitment to the journal and its vision to bring a love of medical research to medical students all around Australia. We wish him all the best with his future endeavours.

Finally, I would also like to take this opportunity to thank our sponsors. It is only with their generous support that our publication continues to be widely available to students across the nation, providing medical students with the opportunity to both publish their research in a high calibre journal as well as to keep up to date with the ground-breaking research work from other Australian students.

To our readers, we thank you again for picking up another copy of the AMSJ. This issue's prize pickings include original research into management of clavicular fractures, a discussion of gender imbalance in ADHD diagnosis, the psychology of hand hygiene and much more.

Turn the page. A world filled with softly beeping cardiac monitors, the cool steel of scalpels, the spreading warmth of hot surgical



Grace Yeung



Karen Du

lights, the hum of doctors at work and the quiet ticking of thinking minds awaits...

Happy reading!

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Medical students and a career in pathology

Adrian YS Lee

Associate Editor, AMSJ

"Medicine is pathology" declares The Royal College of Pathologists of Australasia (RCPA) [1] – a motto that has driven many to delve into this esoteric medical discipline. The legendary Robbins and Cotran textbook elegantly summarises pathology as the study of disease. [2] However, the discipline entails more than just studying disease, since it is firmly integrated in modern medicine through the diagnosis, prognosis, investigation, and management of medical conditions.

The RCPA is responsible for training medical doctors, scientists, and dentists in pathology in Australasia. There are currently nine overarching disciplines that, perhaps unknowingly to medical students, have been covered at various times in medical school: anatomical pathology, chemical pathology, clinical pathology, forensic pathology, general pathology, genetic pathology, haematology, immunopathology, and microbiology. [3] Training to become a pathologist typically takes at least 13 years, including medical school. Some pathology disciplines can also be combined with internal medicine disciplines under the supervision of The Royal Australasian College of Physicians. Because pathologists have medical training, they work closely with both medical practitioners and scientists to provide answers and advice for patients' diagnoses, investigations and management. In addition, as medicine becomes more personalised and predictive at the genetic and molecular levels, [4] pathology will play a more prominent role in patient care. Moreover, pathology laboratories must correspondingly adapt to cater for the analyses of substantial amounts of data. [5] This makes a pathology career a dynamic, fast-paced and challenging area to study and work in.

However, pathology is one of the least popular choices for specialisation, with one survey of Australian trainees showing that only approximately 3% of trainees enter this discipline. [6] Another Australian study found that immunology, as a sub-specialty of pathology, was considered in the top three career choices of only 6% of surveyed final-year medical students. [7] But what makes pathology such an unpopular discipline amongst medical students?

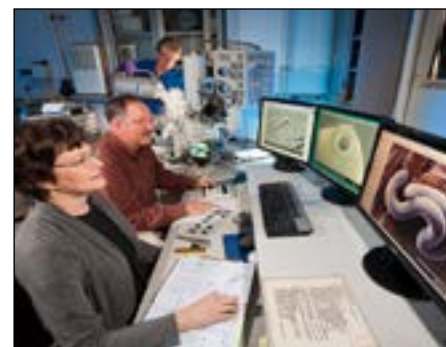
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There have been several reports in the literature looking at this very phenomenon. An early study found that medical students tend to regard pathology with less prestige than other disciplines. [8] Medical students also remarked that pathology was clinically invisible, it was a mere basic science with little clinical applications, and they highlighted negative stereotypes of pathologists, including being "introverts". [9,10] Interestingly, there may be some unfortunate truth to the latter – at least at the student level. A number of studies using standardised psychometric tests found that students who were interested in the hospital-based disciplines (including pathology) scored lower on sociability measures than other disciplines. [11,12]

However, the attractive lifestyle of pathologists appears to be a major advantage, and is well recognised by medical students. [9] But how significant is an attractive lifestyle in influencing one's future career? The limited research suggests that it has become a more dominant factor over the years. [13,14] An early study of United States medical students over a decade found an increasing proportion of the top academic medical students were entering a "controllable-lifestyle" career, including pathology. [15] Resneck has analysed this trend in medical specialty selection and found that this trend reflected a societal shift in people opting for work with more flexibility, and placing more emphasis on friends and family. [16] Thus it appears that external factors are becoming more prominent in dictating ultimate future careers.

Medical students' intended careers are also influenced by their own expectations of future practice, own clinical experiences, influences from peers and mentors, and the exclusion of other disciplines. [9] The impact of role models, too, has a dominating effect on influencing future careers. [17] This influence is certainly important in the field of pathology, where the discipline may not be such an obvious choice for students. [18] Although role models can be junior and senior doctors, the latter (especially consultants) tend to have a bigger influence on future careers, according to one survey of medical students. [19]



One author has even argued that medical schools have a duty to expose students to the field of pathology, since a survey of Canadian residents found many stated that they receive little pathology teaching as a student, and therefore had several misconceptions about the discipline. [20] This suggests that a way for engaging more students and junior doctors in pathology is adequate exposure to the field during medical school. This may be through a stronger emphasis on role models or mentors, or medical school societies that promote interest in the area. Teachers/clinicians may also foster interest through the encouragement of research, by supplying research projects for medical students. [21] As a fast-advancing medical discipline, pathology is an ideal area for students to engage in.

In conclusion, there appears to be a multitude of reasons why people enter or avoid pathology, ranging across internal to external influences. Although it may not be the most popular medical discipline, pathology offers practitioners a challenging career that is advancing quickly as the understanding of genetic, molecular and cellular aspects of medicine are unravelled. So medical students may create an informed evaluation, teachers or role models should ensure adequate exposure of this discipline during medical school.

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Educating tomorrow's global health leaders

Neeranjali Jain and Swaranjali Jain

Associate Editors, AMSJ

One of the six key priority areas identified by The United Nations Global Strategy for Women's and Children's Health is to develop 'stronger health systems with sufficient skilled health workers at their core'. [1] Such skilled workers require an awareness of global health issues in order to meet the challenges inherent in future practice in the modern globalised world. Early exposure to global health experiences as a medical student is important in promoting future global health leadership, and can also help to optimise practice in the local community.

There has been a burgeoning interest in global health amongst medical students. [2] Today's medical students are increasingly aware of global health issues and feel a strong sense of responsibility towards the global community. This can be attributed to numerous factors, including the media, which has forged a sense of an interconnected global society, and the rise of challenges that do not recognise geographic borders, such as climate change and the spread of infectious diseases. [3-5] This has emphasised that global issues are far less remote than they might have once seemed.

For medical students to make meaningful change in the global health arena, they require skills that may extend beyond those taught by traditional medical curricula. The attributes of a global health leader, according to Rowson *et al.*, include being 'globalised', 'humanised', and 'policy-orientated'. [6] Increasing globalisation demands that doctors are culturally sensitive and address determinants of health at global as well as local levels. Overseas medical experiences can encourage 'globalised' thinking, for example by encouraging flexibility as students witness alternative models of care guided by different cultural values. [7] One of the most important driving forces behind students' commitment towards contributing to developing world health is altruism, which underlies practice as a 'humanitarian' doctor. Humanitarianism makes participation in global health rewarding for many, and can foster a lifelong commitment to global health action and leadership. Another less well-recognised attribute of global leaders is the understanding that doctors can have a substantial impact not only through treating individual patients, but also through policy-making at a population level. A key

way Australian health professionals have helped in developing countries has been by advocating in partnership with local leaders to effect change. For example, the TraumaAid International organisation established by Dr Jennifer Dawson equips local leaders to run programs in the community on how to deal with trauma experiences. [8] Closer to home, there have been striking examples of doctors utilising their political voices to protect vulnerable populations, such as through advocacy for the rights of asylum seekers. [5,9]

The skills learnt overseas benefit students by not only encouraging them to be global health leaders, but also to be effective doctors back home. Students have reported enhanced clinical and communication skills, lateral thinking, personal awareness and enthusiasm towards training following overseas elective experiences. [10] They are also more likely to seek to serve underprivileged populations, including in rural and remote Australia. [11] Experience in low-resource settings can also help graduates to be more aware of the impact of their clinical decisions. For example, the principles of the rational use of investigations learnt in developing countries can be transferred back to local settings to promote cost-effective practice by minimising the over-ordering of tests in favour of astute clinical assessment. [10]

A number of initiatives have arisen to meet the growing interest of Australian medical students in global health. Largely student-driven, these include the annual AMSA Global Health Conference and the formation of university global health interest groups which operate within the AMSA Global Health Network. [4] Being part of a global health group encourages students to develop an early passion in global health and network with like-minded individuals to share ideas. [2] Global health groups have also taken leadership in piloting education programs that raise awareness of current global health issues. Encouragingly, these programs attract not only medical students, but also students completing a variety of courses at university and even the general public, as has been our experience with the global course facilitated by the Medical Students' Aid Project at UNSW. This underscores a key reality in global health, that solutions in the developing world often require partnership between medical professionals and those outside the medical sphere.



A popular way in which students gain practical experience in global health is through arranging electives in developing countries. The benefits of such electives are numerous. It is important to note, however, that electives can be associated with potential harm to both the student and the local community. Risks include lack of supervision which can lead to students assuming roles beyond their capabilities, which can compromise patient care. [7] Trainees may also experience physical harm due to unstable environments or psychological impacts which can be exacerbated by limited support networks. [7] The potential harm to local communities can include disruption to local practices and disincentives to governments to invest in local workforces. It is well-recognised that initiating long-term, continuous partnerships with communities are more effective in optimising health outcomes compared with short-term, "bandaid-approach" medical missions. [3] Further strategies to reduce risks and promote ethical practice are discussed in guidelines, such as 'A Guide to Working Abroad for Australian Medical Students and Junior Doctors' by AMSA and the AMA. [12,13] These resources can encourage students to be mindful of their potential impact on communities.

It is clear that an awareness of global health is vital for preparing future doctors to meet diverse future health challenges. Although numerous student-run opportunities exist for students to engage in global health, there has been a call to also integrate global health into the formal university curricula, with over 90% of students believing that global health should be a component of medical school programs. [7,11] This could complement overseas medical experiences by providing a conceptual framework of the global health environment, which can be reinforced by

practical experience.

In our ever-changing environment, it is vital that students and junior health professionals are offered all of the opportunities they require to lead meaningful change in tomorrow's world.

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Conflict of interest

None declared.

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For Euthanasia: Murder versus mercy

Dr Roger Hunt

BM, BS, GDPH, FACHPM, MD

Dr. Roger Hunt is a palliative medicine specialist, working in the discipline for three decades, is a life member of the Palliative Care Council of South Australia, and achieved an MD by published work.

Murder versus mercy?

Under existing law, if a doctor intentionally and compassionately hastens a patient's death, upon the patient's request to end their suffering, that doctor can be prosecuted with the most serious of crimes – murder.

Is this a just law? If you answer 'No . . . the doctor should not be charged with murder', then you favor law reform for voluntary euthanasia (VE). If you say 'Yes . . . the doctor should be prosecuted for murder', then you are against VE reform.

Surveys of Australians over the past few decades consistently show that around 80% believe a person with terminal illness should have a legal option for VE to end their suffering. [1] About 50% of doctors favor law reform. [2] Curiously, it seems palliative clinicians and parliamentarians have the lowest level of support.

I came into palliative medicine with no fixed position on VE, but as I witnessed the suffering of patients, and listened to their wishes, some pleaded with me to hasten their demise. I progressively formed a view in favor of VE reform.

In this short article, I will examine some of the major myths about VE. I will allude to published evidence, including from jurisdictions where either VE or physician assisted suicide (PAS) has been legalized (The Netherlands, Belgium, Luxembourg, Switzerland, and USA – Oregon, Montana and Washington).

Myth: Palliative care relieves suffering so there is no need for VE

The problem is that it is impossible to relieve all suffering. Dying people have varied and sometimes intense suffering, including physical, emotional, and existential suffering. Every survey of hospice patients shows they experience multiple concurrent symptoms. Severe refractory symptoms, including suffocation, pain, nausea and confusion, requiring palliation with deep sedation, have been reported in up to 50% of palliative care patients. [3]

Also, surveys show 5 to 10% of patients with advanced cancer request a hastened demise, and this proportion is actually higher in patients who receive hospice care. [4,5]

In the VE debate, many palliative specialists have difficulty hearing and representing the wishes of their patients who want VE, and difficulty appraising the relevant literature. Does some ideology (perhaps medical or religious) impede their ability? Do they fear being personally involved in VE? Why do they view VE as antagonistic to palliative care?

Myth: Legalizing VE undermines palliative care development

In fact, the opposite occurs - when VE legislation is introduced, palliative care is boosted. For example, in the Northern Territory, as a consequence of debate about The Rights of the Terminally Ill Act, the world's first VE legislation, the NT palliative care service gained the highest per capita funding in Australia. In Oregon, where PAS was enacted in 1997, palliative referrals increased, markers of end-of-life care became among the best in the USA, and over 90% of those who accessed PAS also had hospice care. [6,7]

When VE reform is being considered, the importance of palliative care becomes obvious to parliamentarians and health care administrators, so its development is naturally enhanced rather than undermined.

Myth: Allowing VE creates a 'slippery slope'

This argument suggests doctors will develop a 'lust for killing', that 'a culture of death' will grow, and vulnerable people will increasingly

be pressured to die, or be killed against their wishes (a bleak view of humanity!). Data from more and more jurisdictions, however, indicate the 'slippery slope' is a myth. For example, in the Netherlands, 1.7% of deaths involved VE in 1990, and in 2005 it was the same (1.7%). [8] In Oregon, where 0.2% of all deaths involve PAS, it is educated rather than vulnerable persons who access PAS. [6,7]

Interestingly, surveys in countries that have yet to sanction VE or PAS have higher rates of (covert) voluntary and non-voluntary euthanasia. For example, a survey of Australian medical practice revealed 3.5% of deaths involved 'ending life without explicit request', whereas the comparable figure in The Netherlands was 0.7%. [9]

Also, a survey of Australian surgeons revealed one third had given medications with the intention of causing death, often without request (if the criminal law was thoroughly enacted, there would be a lot of Australian surgeons in prison!). [10]

This raises the possibility that visibility (through reform) may be the best way to protect vulnerable patients.

Myth: Negative effects on the doctor-patient relationship

It is the role of the doctor (conferred by society) to make life-and-death decisions. It is routine for doctors to withdraw and withhold life-prolonging treatments, and to administer medications to relieve suffering, even if death is hastened. Similarly, people want doctors to assist them with VE and PAS.

Doctors in Oregon were more likely to receive an explicit request for assisted suicide if they found caring for a dying patient 'intellectually satisfying', if they sought to improve their knowledge of pain control in the terminally ill, and if they were willing to prescribe a lethal medication. [11] Those who opposed PAS were twice as likely to report patients becoming upset, or leaving their practice, as a result of their position compared with physicians who supported PAS. [11]

We should aim to satisfy the wishes and interests of every patient, and to do our best for each individual that seeks medical help. I think this is why some doctors flout the criminal law, at great risk to themselves, to covertly provide VE for patients in unbearable suffering who plead for such help.

Myth: VE is a form of killing that is unethical

Opponents portray VE as a form of immoral killing, yet there are differences between murder and VE, just as there are differences between rape and making love. A valid moral appraisal must take account of the wishes of the subject, the motivation of the act, and its overall context.

Personal liberty underpins VE - the ability of an individual to make an autonomous choice about the end of their life. VE also requires an act of conscience by the doctor, whose motivation should be compassion and mercy for the person who is suffering and requests help to die.

Conclusion

The overwhelming majority of people want to have a choice about ending their life, should they be suffering with terminal illness. However, the proportion of people with terminal illness who actually want to end their lives with VE or PAS is quite small. Palliative specialists cannot eliminate all the harrowing indignity and disintegration of dying, and should acknowledge the wishes of patients for a hastened demise. Sanctioning VE will promote palliative care; it does not create a 'slippery slope', nor undermine the doctor-patient relationship. It is misguided paternalism that denies patient choice, a lack of mercy that mandates suffering, and an unjust law that puts doctors at risk of

serious prosecution.

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Response to 'Murder versus mercy'

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There is so much misinformation and outdated information surrounding the debate about assisted dying that it is important to try to ascertain what evidence is currently available. Otherwise, myths tend to become 'reality.'

Relief of Suffering

The notion that suffering can be relieved is an attractive one but surprisingly there has been little work undertaken to identify exactly what is meant by the word. Of course, individual suffering is just that – individual. Eric Cassell emphasised the importance of knowing the patient and their values (such as opinions, attitudes, and hopes) in order to try and understand what their suffering is. [1] In Cassell's view, the nature of the illness and the way a patient responds to it reflects the nature of the patient. It is the striving to understand the intricacies of each individual person that makes palliative care such a rich and rewarding discipline. In a systematic review, Best *et al.* [2] revealed that suffering "is multidimensional, oscillating, individual and difficult for individuals to express." They concluded that "opportunities should be provided for patients to express their suffering. The potential for suffering to be transcended needs to be recognized and facilitated by healthcare staff." Euthanasia is certainly a short-cut to ending that suffering, but as Best and colleagues suggest, many people do indeed transcend that suffering in their last days or weeks. We should not give up on trying to help them do that. The idea that severe refractory symptoms causing suffering occur in up to 50% of patients is certainly not my experience over 26 years of practice, and indeed the paper quoted is over 20 years old – many advances have been made over two decades.

The 'Slippery Slope'

More recent data suggest that the slippery slope is indeed a reality. In the Netherlands in 2013 there has been a 15% increase in reported deaths. [3] Somewhat alarmingly, there is an increase "in situations of beginning dementia (from 42 people in 2012 to 97 in 2013) and psychiatric diagnoses (from 14 people in 2012 to 42 in 2013)." [3] The Dutch Review Committees write that "there is an apparent increasing readiness amongst physicians to comply with requests in general and those in case of dementia and psychiatry in particular. It remains difficult to find an unambiguous explanation for this increase in numbers of reported cases." It is also suggested now that around one in five patients choosing euthanasia in the Netherlands act under pressure

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from family members. Professor Theo Boer, one of the supporters of the legislation in that country and a member of a euthanasia Regional Review Committee, who has now recognised the dangers of legalising euthanasia, is also especially concerned about the extension of euthanasia as an option for children – a similar situation to Belgium. Perhaps not surprisingly, assisted dying has also increased in Belgium (by 25% over three years), Washington State (by 17% over 3 years) and Oregon (by 30% in four years). These figures are only for reported assisted dying. It is estimated that under-reporting of euthanasia in the Netherlands represents 20-23% of all euthanasia deaths. A more recent example of the loosening of restrictions on premature ending of life is the development in the Netherlands of a network of traveling euthanizing doctors under the name 'End of Life Clinic.' These doctors do not need a relationship with the patients they see. Will this perhaps just become another easy way to reduce the 'burden' on a family or on society? The British Medical Association has previously stated that "any moral stance founded on the permissibility of active termination of life in some circumstances may lead to a climate of opinion where euthanasia becomes not just permissible but desirable." [4]

Doctor-Patient Relationship

The involvement of doctors in ending a life will necessarily impact on the doctor/patient relationship. This relationship currently is dependent on mutual trust; however, this bond will become increasingly fragile as doctors seek their boundaries in the issue over life and death changing. Assisted suicide offers no second chances. 'Terminal' diagnoses are often wrong or inaccurate in their timing. Perhaps this is why doctors' groups worldwide are persisting in their opposition of law change. Most recently, the British Geriatric Society (BGS) has published a position paper stating that they "do not accept that legalising physician assisted suicide is in the broader interests of society...older people are often strongly influenced by their families and carers – the vast majority, but not all, will have their wellbeing at heart. Even so, many requests to end life...come from the patients' families and not the older person themselves." [5] As the BGS suggest, "crossing the boundary between acknowledging that death is inevitable and taking active steps to assist the patient to die changes fundamentally the role of the physician, changes the doctor-patient relationship and changes the role of medicine. *Once quality of life becomes the yardstick by which the value of human life is judged, the protection offered to the most vulnerable members of society is weakened*".

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Against Euthanasia: Assisted dying is not part of good medical practice

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The issue of assisting or hastening death is not a new phenomenon.

In the 5th century BC, Hippocrates explicitly stated that new physicians must refrain from such a practice. [1] In 21st century practice the majority of jurisdictions around the world still uphold that principle. However, there is increasing pressure from some groups of the public to "have the right to die". What lies behind this movement?

Monforte-Royo *et al.* [2] undertook a systematic review and meta-ethnography from the perspective of patients to try and find out. Their findings are summarised thus: "that the expression of the wish to hasten death...is a response to overwhelming emotional distress and has different meanings, which do not necessarily imply a genuine wish to hasten one's death." Other writers have variously described "total pain", [3] "demoralization syndrome" [4] and "syndrome of end-of-life despair" [5] as being common near the end of life.

The proliferation of hospice and palliative care services worldwide since the late 1960s means that many people now have access to expert help to address these issues, but sadly, not everyone in the medical profession or the public at large feels comfortable dealing with end-of-life issues. Despite the knowledge that every newly qualified doctor will have to deal with upwards of forty people who are dying and their families, in their first year at work as an intern, our medical schools still put little emphasis on this essential element of medical practice.

It is telling that those in the medical profession who are most opposed to assisted dying are those who deal with people who are dying on a daily basis, the palliative medicine physicians. [6] Palliative care is focussed on making the most of each day of life, relieving the burden of troublesome symptoms and addressing psychosocial and spiritual concerns. If practitioners are not properly trained in these areas it is no surprise that some will feel they have no alternative but to acquiesce to a request to assist someone to die. For many, "allowing practitioners to hasten the death of a patient speaks more of abandonment when patients (and their family) need to be drawn together for higher quality of life until death". [7]

In the majority of requests for hastened death, fear emerges as a major theme: fear of imminent death and fear of the process of dying. [2] Similarly, many patients see euthanasia as a way to end suffering – "as a way out or as a means of relieving loneliness, fear, dependence, a lack of hope and the feeling that life [was] no longer enjoyable". [2] In addition, many of these patients see euthanasia as a way of reducing the suffering caused to family and carers. If this is the case, is it not the job of the caring professions at least to attempt to reduce or remove this fear and sense of hopelessness?

Those who work with people near the end of life know what is likely to happen in the process of dying: symptoms can be relieved, explanations can be given, suffering can be addressed and not felt to be too hard to deal with. Rather than rushing to create legislation in an attempt to

address the requests for assisted dying, would it not be better to try and understand the meaning patients in the advanced stages of disease attribute to their suffering and its consequences which render them so vulnerable? And then to ensure that every health care practitioner is equipped to deal with such issues?

Any society can be judged by its ability and willingness to care for those who are most sick and vulnerable. People approaching the end of their life are perhaps amongst the most vulnerable. In addition, an individual's vulnerability to influence and to be made to feel a nuisance or a burden is not unusual. So, how do we assess competence of people who request a hastened death? Reduced mental capacity is common in acutely ill people and yet it has been suggested that clinicians tend not to recognise incapacity. [8] Even in jurisdictions where assisted dying is practiced, psychiatrists have found it difficult to assess whether or not a patient is depressed.

Should the medical profession be involved in the ending of life at all? Many would argue not. It is well established that, amongst those who have been involved with ending life, feelings of emotional discomfort are relatively common. In one study, a proportion of the doctors involved have reported that the emotional burden of having performed euthanasia or assisted suicide had adversely affected their practice. In many ways this is not surprising, as doctors are trained to preserve life, not to end it. [9,10]

Even in countries where the law is clear that an assisted death is permissible, the practical and ethical issues that result from considering and acting upon a request are complex and troubling for most practitioners. [7] The voice of those who would have to do the killing in these circumstances is rarely heard. Perhaps before much further debate into the creation of legislation to support such moves takes place, the role of doctors in this disturbing practice should be made clear.

To accompany people when they are at their most vulnerable and frightened can be hard work, and it is not something that everyone can or will want to do. Each day brings new challenges and opportunities for the patient, their families and their carers. For those who are sick, it is one of the most challenging times of their lives, and yet, paradoxically, it can be one of the most rewarding. The privilege of working with those people and their families is immense. The job of the palliative care specialist and the family medicine doctor is to guide, reassure and comfort not only those who are dying but also those who love and care for them. It is the job of those who accompany people who are approaching death to help rekindle hope, minimize fear and never to abandon them.

Euthanasia, or assisted dying in any form (including assisted suicide), is therefore antithetical to the purpose and practice of medicine as a whole and to the practice of palliative care in particular.

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Response to 'Assisted dying is not part of good medical practice'

Dr Roger Hunt

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Dr. Roger Hunt is a palliative medicine specialist, working in the discipline for three decades, is a life member of the Palliative Care Council of South Australia, and achieved an MD by published work.

I wish to make several points in response:

Relief of suffering

My colleague claims that with 'expert' palliation 'symptoms can be relieved, explanations can be given and suffering can be addressed and not felt to be too hard to deal with'. This is an idealised view that does not acknowledge the limitations of palliative care, and promotes the myth that suffering in terminal illness can be relieved to the extent there should be no desire nor need for VE/PAS.

In reality, it is not possible to effectively relieve fatigue and dependency, or eliminate symptoms caused by failing organs, or change many patients' minds. Evidence indicates that patients receiving specialist palliative care are only marginally better off in terms of symptoms, yet express the wish for a hastened demise more-so than other dying patients. [1]

Patient autonomy

My colleague highlights that patients' requests for VE/PAS are due to 'overwhelming emotional distress', 'total pain', 'hopelessness', 'demoralisation', 'despair', 'fear', 'loneliness', 'vulnerability', 'depression' etc. The argument is that their decision-making capacity is lacking, so there is no need to respect their wishes.

Requests for a hastened demise, however, can be genuine, rational, and in accordance with long-held life values. A person's autonomy is not invalidated because of their suffering.

It is inconsistent and perplexing when respect for patient autonomy is promoted as a core value of palliative care, including for the withholding and withdrawing of life-prolonging treatments, but not when it applies to VE/PAS.

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Effect on clinicians

My colleague suggests that clinicians who become involved VE/PAS are ill-equipped and uneducated in palliative care, and they are adversely affected by ending life.

In Oregon, however, doctors who are actively interested in palliation at the end of life are more likely to be involved in PAS. [2]

Accompanying terminally ill patients with compassion, with respect for their autonomy (the opposite of abandonment), can lead some doctors to be involved in PAS/VE. To borrow the words of my colleague, this "can be hard work, and it is not something that everyone can or will want to do . . . it is one of the most challenging times . . . yet paradoxically it can be one of the most rewarding."

Voluntary euthanasia and palliative care

I agree that we should try to improve education and practice in the art and science of palliation. Evidence indicates that communities that have sanctioned VE/PAS have also enhanced the enterprise of palliation. Palliative care and VE/PAS can be symbiotic rather than 'antithetical'.

Conclusion

In the light of experience in overseas jurisdictions, it is likely that VE/PAS will be legally sanctioned in Australia during your career in medicine. This will empower terminally ill patients with a reassuring choice for a quick exit if their suffering is too great to bear. I am confident the medical profession in Australia will be responsible, careful and considered in the care of patients who request such help to die.

What do you think? Join the discussion on the AMSJ Blog at <http://www.amsj.org/type/blog>. Alternatively, submit a Letter to the Editor to www.amsj.org/submission/submit. Who knows, your letter may be published in the next issue of AMSJ!

New medical school not based on policy

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Kiran is a sixth year medical student at the University of Western Australia, and is the 2015 Western Australian Medical Student Society President. He is actively involved in student advocacy, and is a firm believer and participant in peer education. Kiran has a keen interest in global health policy, and recently completed an Internship with the World Health Organization. He looks forward to his final year of studies, and is hoping for a career in medicine that combines his passions of clinical work and health policy.

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Kate is a third year medical student at the University of Notre Dame, Fremantle, and is the 2015 MSAND President. She previously completed a Bachelor of Economics at the University of Sydney and worked in Industrial Relations prior to beginning medicine. Kate has a keen interest in rural practice and surgery, however she is not yet sure where her career might lead. Kate is looking forward to learning as much as possible in her clinical years.

About AMSA

The Australian Medical Students' Association (AMSA) is the peak representative body for medical students in Australia. AMSA connects, informs and represents students studying at each of the 20 medical schools in Australia by means of advocacy campaigns, events, community and wellbeing projects, and the production of a range of publications.

New medical school not based on policy

The Abbott Government's announcement of a third WA medical school has been met with disappointment from medical students nationally. [1,2] It will exacerbate the bottleneck in medical training whilst doing little to help rural Australia. The decision seems to be more concerned with politics than any real plans to shape a sustainable workforce.

You may consider us hyperbolic, but there is significant truth to our words. Since 2001, medical student numbers have increased dramatically through the establishment of ten new medical schools and the expansion of places at existing schools. [3] In 2013, there were 3,441 medical graduates, over double the 1,400 graduates in 1999. [3] This in turn led to the internship crisis in 2012; for the first time, some locally trained graduates were unlikely to be offered an internship. [4] Through a large #interncrisis social media campaign, and political pressure from opposition political parties, the fated outcome was avoided. [5] Each year since, the Australian Medical Students' Association, in conjunction with their state affiliates, have had to advocate strongly to ensure locally trained graduates are able to secure an internship.

The swell in medical student numbers is having flow-on effects to resident medical officer and specialist training positions. There are too few positions, and those that do exist are heavily oversubscribed. [6] It is therefore disingenuous for the Government to purport that increasing student numbers will somehow solve Western Australia's GP shortage when they have not also funded training positions. [7]

There is a looming bottleneck in the system, with the time taken to become a fully qualified consultant after graduating medical school increasing. [8] From anecdotal evidence, we suspect that this ballooning time is due to an accumulation of junior doctors stuck in their residency unable to enter a speciality training college, including general practice. Unfortunately, there is little data to support this, which is why the AMA Council of Doctors in Training is advocating for a National Training Survey to highlight this likely problem. [9]

Given each of these difficulties, we find it incredulous that the Government has sought to increase student numbers further by

opening a new medical school. The previous expansion of medical student numbers was so rapid and effective that the 2014 Health Workforce Australia report on doctors recommended that "no change should be made to the total medical student intake in 2015". [10] The Government is ignoring its own Department's advice for political gain.

Curtin's proposed medical school is also unlikely to solve the rural doctor shortage.

Australian research has shown that the most effective method of encouraging local doctors to work rurally is to train medical students through a Rural Clinical School (RCS) – a program whereby students spend a year training in rural areas. [11,12] Students who participate in the RCS are twice as likely to work rurally upon graduation. [11,12] Curtin has no plans for a rural clinical school. Instead, the university intends to recruit 20% of their medical student intake from country WA. [13] This however falls short of the WA average (25%), and even shorter of the proportion of population that lives rurally (33%). [3]

There are better fiscal alternatives to promoting rural medicine than opening a new medical school. The Federal and Western Australian State Governments should direct their expenditure to expand the number of RCS places. In Western Australia, there has been unprecedented interest in the RCS with applications to the school exceeding positions two to one. [11] Similarly, rural pathway places for general practice training should also increase. Ensuring that the yearly intake of medical students reflects the rural proportion of the general population could also direct further benefits to rural Australia.

Curtin has put forward the same proposal for a medical school to fix WA's doctor shortage for the past 7 years, yet each year the Federal Health Department has knocked it back as it did not address key concerns. Why has the Government now ignored its own Department's advice and supported it? Let us examine the state and federal electorates in which the new school will be built.

The Federal electorate of Hasluck is held by the Liberal MP Ken Wyatt by a marginal 4.3%. [14] The State electorate of Midland is held by Labor by a mere 24 votes. [15] It begs the question, is the Curtin Medical School about sound health policy or instead votes at the next election?

While the new medical school is slated to open in 2017, it is time we removed politics from the policy planning regarding our future medical workforce. We have described some of challenges to the long-term viability of the medical training pipeline in Australia, and these need to be carefully considered to ensure its longevity for all medical graduates, including those from Curtin Medical School.

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2015 Australasian Students' Surgical Conference research presentations

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Research Convenor

University of Western Australia

The Australasian Students' Surgical Conference (ASSC) is the leading surgical conference for medical students in Australia and New Zealand. ASSC is designed to coincide yearly with the RACS Annual Scientific Conference and was held this year in Perth, Western Australia from 1-3 May 2015.

Organised each year by medical students, in 2015 it provided 250 delegates with a unique opportunity to be educated about, and inspired to pursue, a surgical career through a program of keynote addresses, research presentations and a full day of skills based workshops.

The ASSC committee encourages fellow medical students to develop and challenge themselves professionally. This is a major objective of ASSC, as reflected throughout our entire program. This year, in collaboration with the Australian Medical Student Journal (AMSJ), the winning abstract has been offered publication.

We received an overwhelming response to our call for abstracts, with many outstanding submissions. Abstracts were de-identified, checked for eligibility criteria, and the format standardised prior to consideration by our panel and being offered a podium presentation. Congratulations to our research prize winners:

- Best Research Presentation – Cameron Iain Wells, University of Auckland



Research Presentations

Australasian Students' Surgical Conference

www.assc2015perth.com

1-3 MAY 15

- Runner up Research Presentation – Damian James Ianno, University of Melbourne
- Best Poster Display – Omar Khan Bangash, University of Western Australia

With such a phenomenal response, the 2015 ASSC committee is delighted for other participants to also have their research presented in the AMSJ.

The ASSC committee look forward to seeing you at the next ASSC!

Best research presentation: Anterior resection syndrome – a risk factor analysis

Cameron Iain Wells

Fourth Year Medicine (Undergraduate)
University of Auckland

Cameron Wells is a 4th year medical student at The University of Auckland, New Zealand. He has a keen interest in research, and hopes to incorporate this in his career as a doctor. He was the winner of the Developing a Career in Academic Surgery Prize for 2014, and winner of Best Podium Presentation at the Australasian Students Surgical Conference in 2015

Ryash Vather¹ (MBChB), Michael JJ. Chu¹ (MBChB), Jason P. Robertson¹ (MBChB), Ian P. Bissett¹ (MBChB, MD, FRACS)

¹Department of Surgery, The University of Auckland, New Zealand

Introduction

Evacuatory dysfunction following distal colorectal resection varies from incontinence to obstructed defaecation and is termed anterior resection syndrome (ARS). It has been shown to severely impact postoperative quality of life. Despite this, its precise aetiology remains unclear. This study aimed to identify clinical risk factors for the development of ARS.

Methods

With ethics approval, all anterior resections performed by the colorectal team at Auckland Hospital from 2002-2012 were retrospectively evaluated. An assortment of patient and perioperative variables were recorded. Evacuatory symptoms were manually extracted from surgical follow-up clinic letters. ARS was defined as the presence of any one or more of: faecal incontinence, urgency, stool frequency, incomplete evacuation, constipation, or change in stool consistency. Cases were stratified by occurrence of ARS symptoms from 1-5 years postoperatively. Univariate and regression analyses were then performed to identify independent predictors of ARS.

Results

277 patients were identified. The mean duration of follow-up was 2.71 years (range 1-5 years). The prevalence of ARS decreased progressively from 61% at 1 year to 43% at 5 years. Data extraction was >99% complete for patient and peri-operative variables. Univariate analysis identified anastomotic height, surgeon, pT stage, procedure year and temporary diversion ileostomy as recurring significant correlates ($p < 0.05$). Logistic regression identified lower anastomotic height (OR 2.12, 95%CI 1.05-4.27; $p = 0.04$) and obstructive presenting symptoms (OR 6.71, 95%CI

1.00-44.80; $p=0.05$) as independent predictors at 1 and 2 years respectively. Postoperative chemotherapy was a predictor at 1 year (OR 1.93, 95% CI 1.04-3.57; $p=0.03$). Temporary diverting ileostomy was an independent predictor at 2 (OR 2.49, 95% CI 1.04-5.95; $p=0.04$), 3 (OR 4.17, 95% CI 1.04-16.78; $p=0.04$), 4 (OR 8.05, 95% CI 1.21-53.6 $p=0.03$), and 5 years (OR 49.60, 95% CI 2.17-1134.71; $p=0.02$) after correcting for anastomotic height in the regression model.

Conclusion

Anastomotic height, postoperative chemotherapy and obstructive presenting symptoms were independent predictors at 1 and 2 years. Temporary diversion ileostomy was an independent predictor for the occurrence of ARS at 2, 3, 4, and 5 years after correcting for anastomotic height. Prospective assessment is required for more accurate risk factor analysis.

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Runner-up research presentation: Colonoscopic localisation accuracy for colorectal resections in the laparoscopic era

Raymond Yap

MBBS, FRACS

Cabrini Department of Surgery, Monash University

Raymond Yap is currently a colorectal research fellow at Cabrini Hospital. He has an interest in colorectal cancer research as well as interests in surgical education.

Damian James Ianno

Third Year Medicine (Graduate)

University of Melbourne

B. Biomedicine (Hons)

Damian Ianno is a medical student with a passion for surgery, mental health and writing.

Adele Burgess

MBBS, FRACS

Colorectal Surgery Unit, Austin Hospital

Adele is head of colorectal surgery at the Austin Hospital. Adele's surgical interests include: colonoscopy and gastroscopy, cancer screening, prevention and cancer surgery, laparoscopic surgery (keyhole), diverticular disease management and surgery, management of functional bowel problems including irritable bowel syndrome and constipation, pelvic floor dysfunction management

Introduction

Colorectal cancer resection is increasingly laparoscopically assisted, where intraoperative tumour localisation is more difficult. Incorrect localisation can result in changes to the operation, or incorrect resection of bowel. Few studies look at colonoscopic localisation inaccuracy and its effect on subsequent surgery, especially in the laparoscopic era. This study was designed to evaluate preoperative colonoscopic localisation accuracy, factors that might contribute to incorrect localisation, and the effects on surgical management.

Methods

A retrospective review of prospectively collected data from patients who underwent colonic resection after preoperative colonoscopy between 2008-2013 at a single tertiary hospital was conducted. The primary objective was to investigate whether the colonoscopic and operative locations corresponded. Secondary objectives were to investigate factors surrounding incorrect localisation.

Results

210 patients with 221 lesions were identified. Most lesions corresponded in location on both colonoscopy and at surgery (79%). 9 patients (4%) required a change in operative management due to incorrect localisation. Both the specialty background of the endoscopist and the completeness of the colonoscopy were statistically significant factors associated with incorrect localisation.

Conclusion

Colonoscopy is relatively accurate at localising lesions. Careful collaboration between endoscopists and surgeons is needed to ensure that lesions are correctly localised, or to communicate any doubts in colonoscopic localisation. Adjunct tools such as tattoo should be employed if a lesion that may require further intervention is identified. Further emphasis is needed to ensure that the training of colonoscopy includes awareness of colonoscopic position (including possible protocolisation of colonoscopic location) and on protocols for tattoo use.

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Best poster display: Deep brain stimulation targeting the zona incerta modulates eye movements in humans

Omar Khan Bangash

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The University of Notre Dame
BSc, BMedSci (Hons)

Omar's interest in Functional Neurosurgery led to a dedicated year investigating the effects of posterior subthalamic area deep brain stimulation on human eye movements. This work was assisted by the award of the Sir Hector Stewart scholarship. Currently, as part of the Neurofinity research group led by Prof. Christopher Lind, his interests include advancing the understanding of functional neuroanatomy for therapeutic intervention, the neural basis of complex movement and the fundamental workings of the brain.

Arosha Dissanayake² (MBBS), Shirley Knight³, John Murray³, Megan Thorburn² (GDipN), Nova Thani² (MBBS, FRACS), Arul Bala² (MBBS, FRACS), Rick Stell³ (MBBS, FRACP), Christopher R.P Lind^{1,2} (MBChB, FRACS)

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Departments of ²Neurosurgery and ³Neurology, Sir Charles Gairdner Hospital

Introduction

The posterior subthalamic area (PSA) centred on the zona incerta (ZI) is a promising experimental target for therapeutic deep brain stimulation (DBS). Animal evidence indicates the ZI may play a role in saccadic eye movements via a GABAergic incerto-collicular pathway. PSA DBS for Parkinson's disease (PD) and essential tremor (ET) provided a rare opportunity to test this hypothesis in humans. The effects of PSA DBS on saccades have never been previously characterised.

Methods

Sixteen patients (PD=12, ET=4) underwent DBS using the magnetic resonance imaging (MRI) directed implantable guide tube technique. Active electrode positions were confirmed at the caudal ZI. Eye movements were tested using direct-current electro-oculography (EOG) in the medicated state pre and post-operatively on a horizontal predictive task subtending 30°. Post-operative assessments consisted of stimulation-off constituting a microlesion (ML) condition and high frequency stimulation (HFS: frequency = 130Hz) up to 3 volts. REX/MARK software allowed for analysis of saccade amplitude, peak velocity, duration and latency. A two-way analysis of variance (ANOVA) was performed with $\alpha=0.05$.

Results

PSA HFS leads to significant reduction in first saccade amplitude by 10.4% (95% CI 8.68 – 12.2) and 12.6 % (95% CI 10.0 – 15.9) in the PD and ET groups respectively. With HFS peak velocity was reduced by 14.7% (95% CI 11.7 – 17.6) in the PD and 27.7% (95% CI 23.7 - 31.7) in the ET group. HFS lead to PD patients performing 21% (95% CI 16 – 26) and ET patients 31 % (95% CI 19 – 38) more saccadic steps to reach the target.

Conclusion

Posterior subthalamic area DBS in patients with PD and ET leads to hypometric, slowed saccades with an increase in the number of steps taken to reach the target. Given the location of the active contacts the GABAergic (inhibitory) incerto-collicular pathway is likely to be responsible. This is the first evidence for its existence in humans. Our findings also suggest patients undergoing PSA DBS may have impaired saccadic performance which requires further investigation.

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Gems of the 2015 Australasian Students' Surgical Conference

Evaluation of anti-pseudomonal activity of a range of organic acids and trisodium citrate

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Introduction

Antibiotic resistance is of growing concern and additional effective antibiotic therapies and strategies are required. Weak organic acids, including short chain fatty acids, and salts inhibit and kill a range of microorganisms, a property that has been exploited in food manufacturing and in several clinical settings. This study aimed to characterize the anti-pseudomonal activity of several weak organic acids and a salt.

Methods

The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of a range of weak organic acids (acetic, lactic, propionic, sorbic, succinic) and trisodium citrate salt were determined for 27 clinical and 7 reference isolates of *Pseudomonas aeruginosa*. Serial dilutions of the antimicrobial agents in Mueller-Hinton broth were prepared in 96-well plates. Wells were inoculated with *P. aeruginosa* and incubated at 37°C for 18-24 hours. The MIC was defined as the lowest concentration resulting in no turbidity. Volumes of 10 µl were sampled from wells around the MIC, spotted onto fresh media and incubated at 37°C for 24-48 hours. The MBC was defined as the lowest concentration resulting in no colonies. Attempts were made to generate resistance in three *P. aeruginosa* reference isolates to acetic acid, lactic acid and trisodium citrate by serially sub-culturing 3 isolates in increasing concentrations of agent.

Results

The minimum concentration that inhibited 90% of the isolates tested (MIC₉₀), was determined for each agent. The MIC₉₀ of citric acid was 8 mM, the lowest of all the antimicrobial agents. An MIC₉₀ of 16 mM was recorded for lactic, propionic, succinic and acetic acids. Sorbic acid and trisodium citrate were the least effective inhibitory agents. MBC₉₀ were also determined. Lactic and citric acid were equally the most effective bactericidal agents with MBC₉₀ of 16 mM. The MBC₉₀ of acetic, succinic and propionic acids were 32 mM. The MBC₉₀ of sorbic acid was 256 mM and the MBC₉₀ for trisodium citrate was greater than 32%, the highest concentration tested. Serial sub-culture of bacteria in increasing concentrations of acid or salt did not generate any resistance to these agents over 4 weeks. Periodic MIC determinations, showed no changes in MIC results.

Conclusion

Weak organic acids and trisodium citrate possess useful inhibitory and cidal activity against a range of *P. aeruginosa* clinical and reference isolates and resistance did not develop. These agents represent highly accessible and affordable alternative topical therapies for *P. aeruginosa* infections and may be useful in a range of clinical situations.

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Two cases of isolated rupture of the short head of biceps at the musculotendinous junction

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Introduction

Injury to the biceps muscle has been well documented and occurs most commonly to the long head as described by Gilcreest in his series of 100 patients with known biceps injury. [1] Isolated injury to the short head of biceps is a very rare injury and it was estimated by Postacchini et al that short head rupture occurs in no more than 0.5% of all bicipital tendon ruptures. [2] Furthermore, there have been no published reports of rupture at the musculotendinous junction of the short head of biceps. This report will outline two such cases both occurring whilst water-skiing.

Methods

In 2009 two males (aged 19 and 21) sustained separate water skiing injuries one month apart where the towrope was forced against the flexor region of the arm. Whilst trying to adduct and flex the extended arm, they both sustained complete musculotendinous ruptures of their short head of biceps. Both underwent pre-operative magnetic resonance imaging.

Results

Surgical repair was performed using absorbable sutures. One patient had the short head muscle belly flipped distally to lie in a subcutaneous plane at the level of the elbow. Post-operative management included cast immobilisation for three weeks then gently range of motion exercises. Both patients recovered their full range of motion in the arm. There were no complications.

Conclusion

This is a unique series of complete musculotendinous rupture of the short head of biceps. The mechanism of injury was resisted adduction and flexion against the towrope handle with the arm in extension. These ruptures occurred in high impact, high velocity accidents. Surgical repair lead to an excellent outcome.

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Better off in the bush? A comparison between student surgical learning in rural and metropolitan centres

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Introduction

Rural longitudinal training programs for medical students are now well established and are considered a key component in the push to solve rural health workforce shortages. However, as delivering a surgical curriculum in these sites can be especially challenging, a comparison was made between students' surgical experiences in the rural versus the metropolitan setting.

Methods

Griffith University students in rural (GP led) and metropolitan settings were studied using a mixed methods approach. Each

student underwent a survey and some elected to have a follow-up interview. Their end-of-year surgical examination marks were also compared.

Results

Subjectively, the students (n=69) reported better clinical exposure in metropolitan settings but better procedural and theoretical exposure in rural settings. Rural students reported higher satisfaction with their experience. Interviewees from rural sites (n=16) described opportunities to work-up undifferentiated patients but limited perioperative management experience. Interviewees from metropolitan sites (n=10) described good outpatient exposure but fierce competition for learning experiences. Objectively, the rural students' overall surgical examination marks were modestly but significantly ($P = 0.02$) better than those of their metropolitan counterparts.

Conclusion

Subjectively the rural students felt they had a better surgical experience overall and objectively their examination results were modestly but significantly better. It is likely that student self-selection, scope of practice seen, settings of exposure, and competition for learning experiences all play a part in explaining these results; and lessons can be learned to improve both cohorts' experiences.

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Double gloving in the operating theatre: The benefits and the potential drawbacks

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Matthew Papageorgiou is a third year postgraduate medical student currently studying his MD at Flinders University. Before medical school, Matthew was a student of the medical sciences at Flinders where he was awarded his undergraduate degree in 2012. He currently has interests in the areas of internal medicine, surgery and anaesthetics. He also enjoys fishing.

Introduction: There are potential benefits and drawbacks when double gloving in the operating theatre. Working in the operating room is associated with a high risk of contact with bodily fluids. To prevent breaches of surgical gloves in theatre it has been suggested in the literature that using two pairs of gloves (double gloving) could provide benefit. **Advantages:** Double gloving reduces the amount of contact with the patient's blood and is also effective at reducing the level of exposure to infectious material during needle stick injury. Double gloving also reduces the risk of perforation compared to single gloving. **Disadvantages:** However, it is suggested that double gloving may actually compromise manual dexterity, tactile sensitivity and 2-point discrimination. **Conclusion:** In conclusion, double gloving does provide greater protection against infection transmission than 'single gloving' in relation to intraoperative glove perforation and needle stick injuries, and does not appear to compromise surgical performance.



Introduction

Working in the operating room is associated with a high risk of contact with bodily fluids, especially for surgeons. [1] Transmission of an infection from a patient to a surgeon or other operating room staff occurs through mucocutaneous or percutaneous transmission, such as a needle stick injury. [2] Transmission of blood borne viruses such as hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency virus (HIV) are of particular concern to the occupational health and safety of surgical staff. Infection transmission from the surgical team to the patient may also be of concern. [3] For these reasons it is important to have measures in place for infection control. Use of intact surgical gloves is one way of preventing the transmission of these infections. However, breached gloves allow potential exposure to infectious material, especially if there are cuts or abrasions present. Breached gloves not only indicate potential for mucocutaneous transmission but also promote the possible inoculation of blood from a needle stick injury. [1]

To prevent breaches of surgical gloves in theatre it has been suggested in the literature that using two pairs of gloves (double gloving) is effective in reducing transmission of infection to surgeons and operating room staff. Double gloving is thought to be superior to 'single gloving' as it has a greater resistance to withstand breaches and perforation, lowering the probability of puncture. [1] Furthermore, double gloving is also understood to provide a lower dose of inoculated infectious fluid during needle stick injuries. [2]

This article will examine whether 'double gloving provides greater protection against infection transmission than single gloving during intraoperative glove perforation and needle stick injury'.

Why surgeons double glove

Double gloving reduces the amount of contact with the patient's blood. Blood borne infection may be transferred when bodily fluids and blood are transferred between the surgical staff and a patient, exacerbated by pre-existing cuts or abrasions already present on the skin. One study revealed that pre-operatively, 17.4% of surgeons had skin abrasions on their hands. [1] Furthermore, 38-50% of practicing surgeons may not be adequately immunised against HBV to prevent infection. [13] It has been estimated in a study that double gloving reduced the rate of

blood contamination of the hands from 13% in the single glove group to 2% in the double glove group. [14]

Double gloving is also effective at reducing the level of exposure to infectious material during a needle stick injury. The risk of acquiring an infection from percutaneous exposure after a needle stick injury is 0.3-0.4% for HIV, 6-30% for HBV and 3-10% for HCV. [9] The volume of bodily fluid transferred by the needle itself in a needle stick injury is a predictor of the possibility of infection, with lower volumes providing a lower viral load. [10] A recent study used double gloving and single gloving techniques of the same collective thickness and glove material to determine the amount of contaminate transmitted during simulated needle stick injuries. The results supported that the double gloving technique provides greater protection, with lower levels of contaminate transmitted through the needle stick injury. [2] Hence, double gloving is likely to be effective at reducing the level exposure to contaminate on a needle and consequently may reduce the incidence of transmission of infection to surgical staff. Therefore double gloving reduces the exposure of infectious contaminate on a needle stick during an injury, and may help prevent establishment of an infection, improving occupational health and safety.

The risk of perforation when double gloving is lower than the risk of perforation compared to single gloving. Intact gloves prevent the transmission of infection and therefore are important in the control of infection and safety. An analysis of gloves post-operatively found that 20.8% of surgeons who had single gloved had perforations and exposure to potentially infectious material, but only 2.5% of surgeons that double gloved had tears in the inner and outer glove. [11] A systematic review, including 31 controlled trials, reported that there were significantly more perforations of the single glove than the innermost (closest to skin) of the double gloves (OR 4.10, 95% CI 3.30 – 5.09). [12] Additionally, using an indicator glove (coloured latex underneath a second glove) warns the surgical team of any perforations and allows a replacement of the outer glove, which reduces the probability of tearing both layers and exposure to infectious contaminate. [12] Therefore double gloving protects the surgical staff and the patient from any exposure to potentially infectious contaminate and improves occupational health in the operating room

Why surgeons may not double glove

On the contrary, it has been claimed that the use of 'double gloving'

may actually compromise manual dexterity, tactile sensitivity and 2-point discrimination of the surgeon, therefore reducing the ability and quality of the surgeon's performance. [3] Another problem may be that a decrease of manual dexterity may increase the rate of needle stick injuries. Additionally there is poor acceptance among surgeons to double glove including a regular habit of single gloving, comfort, and low risk of transmission. Furthermore, some choose not to double glove because they feel there is a lack of evidence supporting its protection. [5]

Double gloving diminishes the hand sensibility and moving two-point discrimination of surgeons compared to single gloving, both of these being important for a surgeon to perform to the highest standards. Studies have demonstrated that double gloving does indeed have an effect on hand sensibility when evaluating pressure sensitivity, when compared to a single glove and no glove. Furthermore double gloving was found to impair moving two-point discrimination, but not static two-point discrimination, when compared to single gloving. [6] For this reason some surgeons prefer not to use two pairs of gloves as it can affect their surgical performance in the operating room.

Double gloving does not appear to reduce manual dexterity. Of note, many surgeons that advocate single gloving argue that their dexterity decreases with fatigue. Manual dexterity is defined as the ability to move fingers skilfully, manipulate small objects rapidly and accurately. Some surgeons are also concerned that manual dexterity will be compromised if employing a double glove technique during an operation, and consequently may result in poor performance. However this has been challenged in the literature, which suggests there is no difference in dexterity whether single or double gloving techniques are employed. One study examined the knot tying abilities of individual surgeons wearing one and two layers of gloves and found that there was no statistically significant difference between them. [7] Another study found that there was no substantial impact on manual dexterity, measured by a Perdue Peg-board, in double, single and no glove groups. [3] Therefore the use of double gloving as protection does not impair the quality of the surgeon's performance.

Double gloving does not increase the risk of injuries such as needle stick injuries. A decrease in the level of tactile sensibility and manual dexterity of the surgeon is thought to increase the frequency of needle stick injuries in theatre. However as stated previously, manual dexterity is not compromised by double gloving. Furthermore, a study found that there was no correlation with the frequency of actual injuries and glove perforations compared to the number of glove layers. [8] Double gloving is no more of a risk to injury than single gloving; hence there

are no grounds for it to be an occupational hazard.

Double gloving is not universally accepted by surgeons due to a lack of information and misconceptions. A questionnaire completed by surgeons revealed that most (57%) do not double glove, and that the most common reason not to was because of a perceived loss of manual dexterity. After completing the survey, the participating surgeons were given evidence-based information on the potential occupational health benefits of double gloving and only 23% said they would change their practice. [5] Hence, the majority of surgeons do not accept double gloving even with current evidence and may be at unnecessary risk of infection transmission opportunity. Various surgical specialties have different views on double gloving. Orthopaedic surgeons almost universally utilise double gloving technique due to the inherent risks of mechanical injury, [5] whereas plastic surgeons tend to have lower double gloving rates. [5] Furthermore the age of the surgeon appears to have an impact on double gloving rates with older surgeons often opting for single gloves. Anecdotally most trainees now double glove.

Conclusion

In conclusion, 'double gloving' provides greater protection against infection transmission than 'single gloving' in relation to intraoperative glove perforation and needle stick injuries. The prevention of infection transmission between surgical staff and patients is an important aspect of the occupational health and safety of the operating room. There is clear evidence that double gloving reduces post-operative wound infection. In fact this is much more effective than a 5-minute hand wash. However, it is also important to consider the performance of the surgical team with double gloves. Although manual dexterity is not compromised, hand sensibility and moving 2-point discrimination may be impaired whilst double gloving. Furthermore, even when presented with strong evidence for its beneficial use in practice, surgeons still prefer not to double glove. In summary, there is considerable literature that suggests the use of double gloving reduces the probability of infection transmission in the operating room, and because infection is an occupational danger, it is recommended that surgical staff double glove while performing operations.

Acknowledgements

None.

Conflict of interest

None declared.

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Risk factors for iatrogenic opioid dependence: An Australian perspective

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Hannah is a 4th year medical student at James Cook University. Her interests include public health, mental health and addiction medicine.

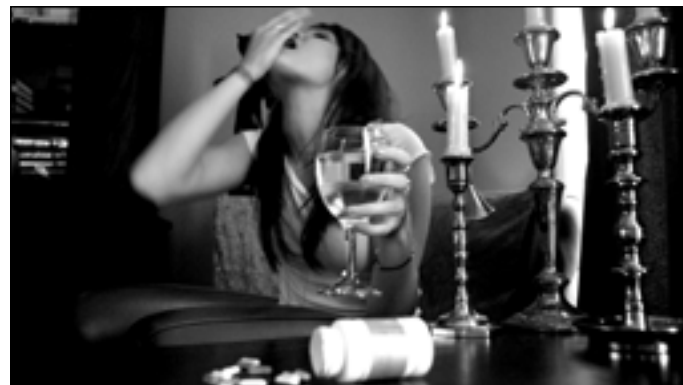
The prescription of opioids is increasing worldwide, including in Australia. Consequently, opioid dependence - one of several harms associated with chronic opioid therapy - is now a growing concern. However, the risk factors for iatrogenic opioid dependence are not well understood in an Australian context. The available Australian evidence for these risks are reviewed and supplemented with data from the United States. Substance use disorder, mental disorder, pain severity and several demographic factors are associated with increased risk of opioid dependence. Factors originating within the health system, such as prescribed dose, chronicity, monitoring systems and physician attitudes may also contribute to patients developing dependence. Australian data represents a significant gap in the knowledge, and there is a need for good quality studies examining Australian populations.

Background

The rate of opioid prescribing both in Australia and worldwide has increased dramatically. [1-3] Opioid-like analgesic dispensing in Australia increased 53% between 2002 and 2009, with tramadol and oxycodone showing the largest increases. [1] This prescribing pattern is of concern since chronic opioid therapy is associated with multiple harms, including dependence and accidental overdose. [4,5] In the USA, prescription opioid-related deaths increased 68% between 1999 and 2003, [6] with the highest risk of death in patients who were prescribed high dose opioid therapy. [7] This trend has been mirrored to a lesser extent in Australia, with an increase in oxycodone-related deaths but not morphine-related deaths. [2] There is evidence that harms related to opioid therapy are increasing as a result of increased prescriptions. [2,8]

Iatrogenic dependence can be described as physician initiated inadvertent dependence. [9] The risk of iatrogenic opioid dependence is unknown and estimates differ greatly between acute and chronic settings. [4,10,11] In addition, opioid therapy trials tend to focus on efficacy and exclude individuals at high risk of dependence. [12] Despite these limitations, studies of patients taking chronic opioid therapy found a 35% lifetime prevalence of dependence. [4,13] As a consequence, iatrogenic opioid dependence is of concern for health professionals and balancing benefits with risk of dependence is a key clinical issue. [8,14,15]

The terminology used to define and describe the use of opioids is controversial. [16,17] There are two main diagnostic systems for the diagnosis of drug use disorders internationally. The DSM-V describes "substance use disorder" as a mild to severe state of chronically relapsing, compulsive drug taking. [18] The International Classification of Diseases (ICD-10) defines a "dependence syndrome" as a cluster of physiological, behavioural and cognitive phenomena in which the use of a substance takes on a much higher priority for a given individual than other behaviours that once had greater value. [19] Addiction is a term widely used by the general public, health professionals and in the literature. [17] It is described as a chronic condition characterised by behaviours such as compulsive use, continued use despite harm and craving. [16] It has been argued that the term "addiction" represents a variety of social and cultural constructs and is often value-laden. [17] For this reason, the term "dependence" is often preferred. [17] In this article, dependence will be used to describe a diagnosed drug use disorder. Readers should view dependence as distinct from physical



dependence, tolerance, abuse and misuse, which are clarified in Table 1.

Table 1. Definition of terms commonly used in the literature relating to opioid dependence.

Term	Definition
Dependence	A diagnosed drug use disorder characterised by a pattern of maladaptive behaviours, such as loss of control over use, craving and preoccupation with non-therapeutic use, and continued use despite harm. [17]
Addiction	A commonly used term to describe a condition characterised by craving and continued use despite harm. [16] Sometimes not preferred due to associated stigma. [17]
Dependence syndrome	ICD-10 diagnostic term. Describes a cluster of physiological, behavioural and cognitive phenomena in which the use of a substance takes on a much higher priority for a given individual than other behaviours that once had greater value. [19]
Substance Use Disorder	DSM-V diagnosis to describe a mild to severe state of chronically relapsing, compulsive drug taking. [18]
Tolerance	The physical adaptation of the body such that more drug is required to reach desired effect. [16]
Physical dependence	Characterised by the presence of a withdrawal syndrome on abrupt cessation or rapid dose reduction of a drug. [16]
Misuse	Use of a drug in a way other than prescribed intentionally or unintentionally. [18]
Abuse	Misuse with medical, social or legal consequences. [18]

Guidelines for the prescription of opioids are conflicting, with confusion around safety and efficacy. [20,21] The United States has the highest rates of opioid use in the world and multiple reviews have examined the potential risk factors for addiction. [22,23] However, differences in prescribing, demographics and health system characteristics indicate that a review in an Australian context is of value. [1] This article summarises the available Australian evidence on the risk of iatrogenic opioid dependence, supplemented with studies from the US. Four major groups of patient risk factors are described: substance abuse

disorder, mental disorder, pain severity and demographic factors. The role of dependence risk screening tools is briefly assessed. Finally, the contribution of specific health system and prescribing factors is discussed.

Methods

A literature search of publications relating to risk factors for prescription opioid dependence was undertaken. The databases PubMed, CINAHL and Ovid were searched for publications published between 2004 and 2014. The search terms "Opioid OR Opiate" and "Dependence OR Addiction" and "Prescription" and "Risk" were used. This search yielded 205 publications. Additional articles were obtained from bibliographic searching. 39 relevant articles were included. 166 articles were excluded as they studied heroin use or focused on harms other than dependence, such as abuse or misuse.

Patient Factors that Increase Risk

Substance use disorder

Despite substance abuse being a strong predictor for opioid dependence, Australian data on the relationship is lacking. Cross-sectional studies from the United States demonstrate a strong correlation between substance abuse disorder and chronic opioid use. [24,25] In addition, evidence suggests that opioid dependence is more likely in those with a past or current substance abuse disorder. [4,8,26,27] This is consistent with a longitudinal study in which a diagnosis of non-opioid substance abuse was the strongest predictor of opioid dependence in those commencing opioid therapy. [15] Recent studies also demonstrate an association between smoking and opioid dependence, with one citing smoking as the most frequently reported risk factor in their cohort. [28,29] No Australian studies were found that examined this relationship. However, the Australian National Drug Strategy Household Survey reported that 36% of recent users of opioids for non-medical reasons also used cannabis and 25% had used alcohol. [30] This data should be interpreted cautiously, as it does not reveal if the use was chronic or acute, or the reasons for use. At best it shows a tendency for opioids to be used with other psychoactive substances.

Mental Disorders

Mental disorders increase the risk of iatrogenic opioid dependence. This is demonstrated by the fact that prescription opioid use is greater for patients with depression and anxiety. [25] Furthermore, these patients were prescribed opioids in higher doses and for longer durations than patients without a mental disorder. [24] Patients with mental disorders also have a higher incidence of chronic non-cancer pain. [24] Whether chronic pain is the cause or result of mental disorders is unknown; some evidence suggests the relationship is bidirectional. [24] Whether more opioids are prescribed to these patients on the basis of their higher reported pain remains to be established.

The outcomes of opioid treatment for patients with mental disorders are not well characterised as these patients are usually excluded from clinical trials. [31] However, several studies show that mental disorders are significantly associated with opioid dependence. [4,8,15,26,27,29,32] Furthermore, having two comorbid mental disorders increases the risk of addiction compared to a single mental disorder. [8] One study found a correlation between PTSD severity and opioid use, suggesting that severity of symptoms may also be implicated. [33]

Despite the increased risk of opioid dependence with mental disorders, one longitudinal study of fifteen thousand veterans with chronic prescription opioid use in the United States showed that only 3% of pain patients with comorbid mental disorders progressed to opioid abuse or dependence. [15] This highlights that the presence of a mental disorder alone cannot predict a patient's risk of developing dependence to a prescribed opioid. There is a lack of Australian data establishing a link between mental disorders and opioid dependence.

Patient Demographics

There are a number of demographic factors that may increase the risk of a patient developing opioid dependence. Studies conducted in the US have identified younger age as a strong predictor of opioid dependence, with individuals under 65 showing increased risk. [4,8,15] In Australia, the National Drug Strategy Household Survey (NDSHS) found that use of opioids for non-medical purposes was highest in persons ages 20-29. [30] As in other substance use disorders, men are more likely to develop opioid abuse or dependence than women. [8,15,26] This is consistent with NDSHS, which found that men were more likely to use pharmaceuticals for non-medical purposes in their lifetime. [30] Several other factors such as living rurally and early age of exposure to nicotine, alcohol and other drugs are significantly associated with opioid dependence. [27] In addition, a family history of substance use disorder and time spent in jail may increase the risk. [26] Being divorced, single or separated and childhood emotional trauma are also associated with opioid dependence. [4,15] It is possible that these factors interrelate and are thus more likely to occur together, compounding the risk.

A recent Australian study analysed data from the Bettering the Evaluation and Care of Health (BEACH) program, which collects data on interactions patient consultations in general practice. It found that Commonwealth Concession Card holders had a significantly higher rate of opioid prescribing compared to other patients. [34] This data poses an interesting question as to why opioid prescribing in this population is higher. Possibilities include increased willingness of doctors to prescribe and lack of access to alternative treatments such as physiotherapy.

Pain severity

The severity of a patient's pain may contribute to opioid addiction. [35] Persistent use of opioids for chronic pain is associated with severe or very severe reported pain. [36] In addition, opioid-dependent individuals show a greater degree of pain-related limitation and greater pain severity. [4,26] This may be because addiction lowers the pain tolerance, or that a lower pain threshold confers an increased risk of addiction. [26,37] Alternatively, people experiencing greater pain severity may simply be prescribed higher doses of opioids. This could also be due to opioid-induced hyperalgesia, a state of nociceptive sensitization caused by exposure to opioids. [38] This can be mistaken for tolerance, which may result in a higher dose of opioids prescribed and thus an increased risk of addiction. No Australian studies were found examining the relationship between pain severity and increased risk of addiction.

Screening for Risk

Ultimately, established risk factors should be used to create reliable screening strategies. While that is considered good practice, there is no one screening procedure that can identify chronic pain patients at risk of opioid dependence. [21,22] A common issue is the overlap of behaviours also seen in patients with undertreated pain, such as demand for higher dose medications, and taking medication in a way other than prescribed (defined as misuse). [22] This is further complicated by the fact that established risk factors have been found to be poorly associated with aberrant drug behaviours. [29]

The Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R, <https://www.painedu.org/soapp.asp>) tool is a self-administered 24-item tool assessing common risk factors for opioid misuse, abuse and dependence. [39] The items assess mood, attitudes towards treatment, personality traits and substance use disorder. [39] A recent study found the SOAPP score to be the strongest predictor of dependence in a cohort of patients using over the counter and prescription painkillers. [40] In addition, Butler et.al found the SOAPP-R to be reliable and valid across two different chronic pain patient populations. [39,41] However, the usefulness of SOAPP-R in a primary health care setting remains to be determined. [39]

The American Society of Interventional Pain Physicians does not recommend the use of formal dependence risk screening tools. [21] In their recent guidelines for responsible opioid prescribing, they suggest that risk stratification can be achieved through a comprehensive physician's assessment. [21] This should include psychosocial history, functional status, psychological evaluation, substance abuse history and physical exam. [21]

Health System Factors Contribute to Risk

In addition to patient factors, there are multiple health system factors that contribute to prescription opioid dependence. These are prescribing dose, duration of therapy, monitoring systems and physician attitudes.

Few studies have examined the relationship between dose and duration of therapy and risk of dependence. However, in a large cross-section study of individuals with a new episode of chronic non-cancer pain, those prescribed high morphine equivalent dose (120 mg), chronic (>90 days) opioid therapy were 50 times more likely to develop dependence than those on low dose acute therapy. [8] This is consistent with a recent study, which found the odds ratio for developing dependence with high dose, chronic opioid use was 122.45. [11] While the rate of high dose chronic opioid prescription in this sample was relatively low (0.1% of chronic pain patients), it represents a number needed to harm of 16.7. [8] Given the significant negative consequences of opioid dependence this number needed to harm may be unacceptable. Multiple studies found that duration of opioid therapy was more important than daily dose in determining risk of dependence. [8,11,42] Indeed, data suggests that other risk factors such as younger age and comorbid mental disorders contributed less to the risk than dose and chronicity alone. [8] This is supported by another study which found that greater than 211 days of prescribed opioids was more predictive of dependence than 90-211 days. [15] Importantly, this also suggests that the association between risk and chronicity is a linear relationship. In Australia stronger formulations account for the minority of opioids prescribed. [2] However, more research into the relationship between opioid dose, chronicity and dependence is required.

One of the goals of responsible opioid prescribing is adequate monitoring, due to the consequences of duration mentioned above. [5,21] Existing monitoring systems in Australia cannot track opioid prescriptions and supply down to the individual patient level. [5] The Pharmaceutical Benefit Schedule (PBS) data set generates a Medicare file, which can potentially identify patients misusing opioids. [5]

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However, no information is included in the PBS record if a patient pays the entire cost of the medication. [5] Lack of access to comprehensive information can contribute to inappropriate prescribing. [43] Thus, a real-time prescription coordination program making use of technology would be greatly beneficial. [43]

Physician attitudes towards opioid analgesics may also profoundly impact on treatment. [14] In a mailed survey to General Practitioners in Ontario, GPs who did not believe many patients became addicted to opioids also prescribed more opioids. [14] Furthermore, over 10% of GP's were not confident in their skills prescribing opioids. [14]. Surveys of Australian physicians studying attitudes to the use of opioids are required. Regardless of the attitude of physicians towards opioid prescription, there remains a responsibility to manage patients' pain effectively. It is well recognised that this poses an ethical dilemma to the treating physician and involves a careful balance of risk and benefit. [9, 44] Several guidelines are available to clinicians to increase their confidence in prescribing opiate analgesics, including the RACP [45] and Hunter New England guidelines. [46]

Conclusion

It is apparent that individuals with highest risk of iatrogenic dependence will possess a constellation of risk factors. A combination of young age, depression, psychotropic medications and pain impairment combined with substance use history predicted greatest increased risk for opioid dependence. [4] However, methods for screening risk remain unreliable, compounded by a lack of universal guidelines to guide practice. In addition, high dose, chronicity, monitoring systems and physician attitudes may also increase the risk of dependence in the population. Thus far, Australian studies into opioid use have described trends in prescribing practices. Studies examining risk factors for iatrogenic opioid dependence represent a significant gap in the knowledge. Further research is likely to help guide clinicians to make better-informed decisions around opioid prescribing.

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Conflict of interest

None declared.

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Perioperative glycaemic control in diabetic surgical patients – review

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Glycaemic control around the time of surgery is a critical part of surgical care in diabetic patients. There is a high prevalence of diabetes mellitus worldwide, and the disease is becoming more common in both medical and surgical patients. Even in patients without diabetes, surgery disrupts usual diabetic management and glucose homeostasis, often resulting in perioperative hyperglycaemia. Hyperglycaemia has been associated with increased postoperative mortality and morbidity, as well as worse surgical outcomes in both cardiac and non-cardiac surgery. Published evidence suggests that outcomes can be improved in perioperative patients by closer management and control of glucose.

Despite early studies in the intensive care unit (ICU) setting, subsequent trials were not able to demonstrate improved outcomes with the use of intensive insulin therapy, which aimed for stricter glycaemic control (4.5–6.0 mmol/L) that was closer to physiological ranges. Whilst the optimal blood glucose concentrations are still unknown, current literature supports the use of moderately strict glycaemic control (5.0–10.0 mmol/L) via a basal-bolus insulin regimen, so as to balance the risks of inducing hypoglycaemia with the benefits of avoiding hyperglycaemia.

Introduction

Diabetes mellitus is a highly prevalent group of metabolic diseases worldwide, and a significant proportion of surgical patients are diabetic. [1] An important component of diabetic perioperative management is glucose control, as glucose homeostasis is easily disrupted during periods of physical stress and illness. Recent studies have shown that hyperglycaemia during surgery is not a benign condition like it was once considered to be, and that treatment results in reduced mortality and morbidity. This literature review will focus on the current understandings of the effects of diabetes, how hyperglycaemia can affect clinical outcomes in the surgical setting, and the present consensus on the management of blood glucose in diabetic patients perioperatively.

Methods

This literature review is constructed as an unsystematic narrative review. The search for current literature was performed through the Ovid Medline database, the PubMed database, and the Cochrane Library. The following search terms and their related terms were used: perioperative glycaemic control, perioperative hyperglycaemic, perioperative diabetic management, intensive insulin therapy, sliding-scale insulin, basal bolus. The articles evaluated were limited to publication between January 1st, 2000 and March 1st, 2015. Articles published were restricted to the English language and to the adult surgical population. Given the breadth of literature on the topic, only major influential studies were selected for review. Studies performed on highly specific populations were excluded. Relevant retrospective observational studies, RCTs, and meta-analyses were included for analysis. Published review articles and editorials were examined for major influential studies. Any relevant in-text citations were also considered for inclusion. In total, forty-seven (n = 47) articles were selected for full text retrieval after abstract screening.



Background

Epidemiology

According to the Australian Institute of Health and Welfare, approximately 900 000 Australians have diabetes. [2] However, it has been estimated that up to half of all cases remain undiagnosed. [3] Similarly, the International Diabetes Federation estimates that diabetes prevalence in the adult Australian community is 9.99%. [4] Type 2 diabetes is the most common variant, accounting for 85–90% of all diabetics. [5] An audit across eleven hospitals in metropolitan Melbourne indicated that 24.7% of all inpatients had diabetes, with prevalence ranging from 15.7% to 35.1% in different hospitals. [6] Given the predicted exponential rise in obesity over the next decade and the current trend of an ageing population, projections suggest that 3.3 million Australians will have type 2 diabetes by 2031. [7]

Pathophysiology of diabetes

Although pathogenesis differs for the various forms of diabetes mellitus, hyperglycaemia is an underlying mechanism by which the disease can cause long-term complications. Diabetes is characterised by a lack of, or reduced effectiveness of, endogenous insulin, which then results in elevated fasting blood glucose concentrations and an inadequate response to glucose loads. Glucose homeostasis is tightly regulated, with normal blood glucose values being maintained within a narrow range between 4.4–7.8 mmol/L. [8] Chronic concentrations above 7.0 mmol/L are capable of producing end organ damage. [9]

Left untreated, diabetes mellitus is a disease associated with acute and chronic organ dysfunction and failure. Persistent hyperglycaemia leads to morbidity mainly through damaging medium and large-sized arteries (macrovascular disease) and causing capillary dysfunction in end organs (microvascular disease). Macrovascular disease increases the risk of developing ischaemic heart disease, cerebrovascular disease, and peripheral vascular disease, while microvascular disease results in diabetic retinopathy, nephropathy, and neuropathy. [10]

Diabetes and surgery

Given the high prevalence of diabetes seen in the community and hospitals, we can expect a significant proportion of those who present for surgery to have the diagnosis. Diabetic complications such as ischaemic heart disease and diabetic eye disease also increase the likelihood of requiring surgical interventions, and it has been estimated that 50% of all diabetic patients will undergo surgery at some stage. [11] The prevalence of cardiovascular diseases, including hypertension,

coronary artery disease and stroke, are two to four times higher in diabetic patients, compared to non-diabetics. [12] Diabetes is also the leading cause of end-stage renal failure, adult-onset blindness, and non-traumatic lower extremity amputations.

In addition, diabetes puts patients at a higher perioperative risk for adverse outcomes when compared to non-diabetics. Mortality has been reported to be up to 50% higher than that of the non-diabetic population. [13] Diabetic patients are also more likely to develop postoperative infections, arrhythmias, acute renal failure, ileus, stroke, and myocardial ischaemia. [14-16] Due to the wide range of complications that can occur, diabetic patients have a 45% longer length of stay postoperatively, with higher health care resource utilisation, compared with non-diabetic patients. [17]

Diabetic patients are prone to dysregulation of glucose homeostasis, especially during surgical stress or critical illness. Since most surgical patients will need to fast prior to surgery, there is often considerable disruption to their usual diabetes management routine. About 20% of elective surgical patients demonstrate impaired fasting blood glucose concentrations. [1] Other factors such as postoperative infections and emesis can all lead to labile blood glucose concentrations. Meanwhile, both surgery and anaesthesia produce a hypermetabolic stress response by elevating the levels of stress hormones and inflammatory cytokines such as catecholamines, cortisol, growth hormone, and TNF- α . [18] These hormones increase blood glucose concentrations by upregulating hepatic gluconeogenesis and glycogenolysis, as well as exacerbate insulin resistance and decrease insulin secretion. [18]

Discussion

Effects of perioperative hyperglycaemia and benefits of glycaemic control

Hyperglycaemia is a prevalent phenomenon in surgical patients. One study found that 40% of non-cardiac surgery patients had a blood glucose concentration >7.8 mmol/L, with 25% of those patients having a blood glucose concentration >10.0 mmol/L. [19] Perioperative hyperglycaemia was once considered to be a beneficial physiological adaptive response to surgery and critical illness, intended to supply energy to vital organs. This is now largely known to be untrue, with observational studies and randomised controlled trials indicating that improvement in glycaemic control results in lower morbidity and mortality, shorter length of stay, and fewer complications such as nosocomial infections, postoperatively. Outside of surgery, hyperglycaemia has also been associated with worse outcomes in critically ill, hospitalised patients. [20] Patients who are hyperglycaemic following a stroke demonstrate worse functional recovery and higher mortality compared to patients with normal glycaemic control. [21]

Retrospective observational studies

An observational study on patients undergoing non-cardiac surgery by Frisch *et al.* demonstrated that perioperative hyperglycaemia is associated with significantly increased risk of pneumonia, sepsis, urinary tract infection, skin infection, acute renal failure and death during the postoperative period. [19] Ramos *et al.* found a correlation between blood glucose concentrations and the rate of postoperative infection and length of hospital stay in general and vascular surgical patients. The study observed that every 2.2 mmol/L rise in postoperative blood glucose concentration above 6.1 mmol/L resulted in an increase in the infection rate by 30%. [22] In cardiac surgery, Gandhi *et al.* observed that intraoperative hyperglycaemia is an independent risk factor for post-operative complications, including death. [23] Schmeltz *et al.* demonstrated that the use of a combination of IV and subcutaneous insulin to improve glucose control in cardiac surgery reduced the mortality and infection rates among diabetic patients to those of non-diabetic patients. [24]

Hyperglycaemia has been shown to be the significant risk factor for perioperative morbidity and mortality, rather than diabetes itself. A retrospective cohort study based on 11,633 patients by Kwon *et al.*

found that perioperative hyperglycaemia was associated with a near doubling in the risk of infection, mortality, and operative complications in both diabetic and non-diabetic general surgical patients. [25] A retrospective study by Doenst *et al.* concluded that a high peak blood glucose concentration during cardiopulmonary bypass was an independent risk factor for death and morbidity in diabetic patients. [26]

Prospective randomised controlled trials

A prospective randomised controlled study of surgical ICU patients by Van den Berghe *et al.* in 2001 (first Leuven study) demonstrated significantly reduced morbidity and mortality in critically ill patients when the blood glucose concentrations were maintained between 4.4–6.1 mmol/L via an intravenous insulin infusion. [27] In another randomised prospective study by Lazar *et al.*, 141 diabetic cardiac surgery patients were assigned to either moderately tight glycaemic control (6.9–11.1 mmol/L) with a glucose-insulin-potassium (GIK) regimen, or to standard therapy (<13.9 mmol/L) using intermittent subcutaneous insulin. [28] The GIK patients had a lower incidence of atrial fibrillation and a shorter postoperative length of stay, compared to patients receiving standard therapy. The intervention was commenced prior to anaesthesia, and only continued for 12 hours postoperatively. Interestingly, the GIK patients were able to demonstrate a survival advantage two years postoperatively, with decreased episodes of recurrent myocardial ischaemia and fewer recurrent wound infections. This suggests that moderately tight control even for a brief period can make substantial differences to long-term outcomes.

The Diabetes Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study by Malmberg *et al.*, which looked at 620 diabetic patients post-acute myocardial infarction, reported a 29% reduction in the 1-year mortality rate in patients who were randomised to receive intensive glucose management (mean blood glucose concentration of 9.6 mmol/L at 24 hours) when compared to patients assigned to receive conventional treatment (mean blood glucose concentration of 11.7 mmol/L at 24 hours). [29]

The question of whether the insulin therapy itself or the treatment of hyperglycaemia resulted in benefit has not been fully answered, as the metabolic and cellular actions of insulin may contribute to the beneficial outcomes. Insulin therapy has been shown to improve dyslipidaemias and prevent endothelial dysfunction and hypercoagulability in critically ill patients. [30] Treating a patient with insulin causes arterial vasodilation and capillary recruitment, via activation of the nitric oxide pathway and improves myocardial perfusion. [31] However, the first Leuven study found that the positive effects of intensive insulin therapy were related to the lower blood glucose concentrations, rather than insulin doses. [27]

Intensive versus conventional glycaemic control

Beyond avoidance of marked hyperglycaemia and hypoglycaemia, the optimal perioperative glucose targets are unclear. Conventional glycaemic control targets blood glucose concentrations <10.0 mmol/L, and there has been considerable controversy over the safety and efficacy of intensive insulin therapy (IIT), which aimed at a much lower and narrower concentration between 4.5–6.0 mmol/L. Despite early results, which suggested decreased mortality and other advantages of intensive glucose control, [27] later investigations found no benefits or increased mortality when hyperglycaemia was aggressively treated with insulin. [32-33] The current consensus is that intensive control does not actually confer any benefits with regards to mortality, but increases the risk for hypoglycaemia, which is a potentially life-threatening complication. [34] The brain is an obligate glucose metaboliser, hence neurons are particularly vulnerable to low blood glucose concentrations. Even brief periods of hypoglycaemia (i.e. blood glucose concentration <2.2 mmol/L) can induce arrhythmias, cardiac events, and brain injury. [35]

The first Leuven study published in 2001 by Van den Berghe *et al.*

demonstrated significant reductions in morbidity and mortality (by 34%) in over 1500 surgical ICU patients with tight glycaemic control (4.4–6.1 mmol/L) when compared to conventional control (<10–11.1 mmol/L). [27] Intensive insulin therapy (IIT) was also shown to decrease the duration of mechanical ventilation and ICU length of stay. However, there were many study limitations that could have affected the validity of the results. Many subsequent randomised controlled trials and meta-analyses that were published contrasted with the initial Leuven study, finding no benefit when IIT was used for glycaemic control, as well as a significantly higher risk of hypoglycaemia. [32–34]

A second Leuven study published in 2006 by Van den Berghe *et al.* was a randomised controlled trial comparing IIT and conventional therapy in 1200 medical ICU patients, and it did not demonstrate any mortality benefit with intensive insulin therapy, while observing more prevalent hypoglycaemic events in the treatment group. [32] Kujik *et al.* observed that intensive glucose control in the perioperative period has no clear benefit on short-term mortality in patients undergoing major vascular surgery, and recommended that moderate tight glucose control be regarded as the safest and most efficient approach to patients undergoing surgery. [36] Duncan *et al.* found that in cardiac surgery, although severe intraoperative hyperglycaemia (>11.1 mmol/L) was associated with higher risk of mortality and morbidity, blood glucose concentrations closest to normoglycaemia (average of 7.78 mmol/L or less) were also associated with increased mortality and morbidity. [37] In fact, the lowest risk of adverse outcomes was observed in the range between 7.8–9.4 mmol/L, suggesting that mild hyperglycaemia was better tolerated than strict control. The association of tight blood glucose control with worse outcomes was observable despite rare episodes of hypoglycaemia, which suggests that there are factors other than hypoglycaemia that could contribute to the poor outcomes of intensive glucose control.

The largest and most definitive study to date is the Normoglycaemia in Intensive Care Evaluation – Survival Using Glucose Algorithm Regulation (NICE-SUGAR) study, which was a multicentre, international, randomised controlled trial aimed at comparing intensive insulin therapy (4.5–6 mmol/L) with conventional treatment (8–10 mmol/L). [33] The study reported a higher 28-day and 90-day mortality rate in surgical ICU patients who received IIT, with significantly more severe hypoglycaemia in those patients. The authors were not able to demonstrate a difference in hospital or ICU length of stay, length of mechanical ventilation, or the need for renal replacement. In contrast to the initial Leuven study, mortality rates were higher in the IIT group (27.5% vs 24.9%). The NICE-SUGAR trial also reaffirmed a higher incidence of hypoglycaemia in the IIT group.

A Cochrane meta-analysis of 12 randomised trials (1403 patients with diabetes) comparing intensive (blood glucose concentration of <6.7 or <8.3 mmol/L) versus conventional (variable) glycaemic control by Buchleitner *et al.* also found that intensive glycaemic control has no significant effect on infectious complications, cardiovascular events, or mortality, except for increasing the number of hypoglycaemic episodes. [34] Given the current data available from randomised controlled clinical trials, the authors concluded that intensive glycaemic control protocols with near-normal blood glucose targets cannot be generally recommended for patients with diabetes undergoing surgery.

Basal-bolus versus sliding scale insulin

Insulin is generally the preferred method of treatment for inpatients as it is an effective medication for immediate control of hyperglycaemia in the hospital setting. The dose can be titrated more rapidly than that of oral hypoglycaemic agents, and it does not have a dose ceiling. Insulin can be delivered either subcutaneously or intravenously as a continuous infusion, and the use of sliding-scale insulin (SSI) has traditionally been the mainstay of hyperglycaemia therapy. However, recent studies have shown that the use of SSI alone is insufficient in providing adequate glycaemic control, and that a combination of basal and supplemental insulin is a more effective approach.

The combined use of basal insulin (i.e., intermediate- to long-acting insulin) together with short- or rapid-acting insulin before meals is able to better mimic physiological patterns of glucose control. The RABBIT 2–Medical trial by Umpierrez *et al.* demonstrated an improvement in glycaemic control with basal-bolus insulin in 130 diabetic insulin-naïve medical patients, with no increase in the number of hypoglycaemic events. [38] The subsequent RABBIT 2–Surgical trial, which is a multi-institutional randomised trial that looked at 211 type 2 diabetic general surgical patients, also found improved glycaemic control and reduced hospital complications with the basal-bolus regimen when compared to the sliding-scale insulin regimen. [39] The most recent evidence suggests that both medical and surgical type 2 diabetic patients with poor glycaemic control (blood glucose concentration >10 mmol/L or HbA1c >7.5%) should be treated with the basal-bolus insulin regimen. [40]

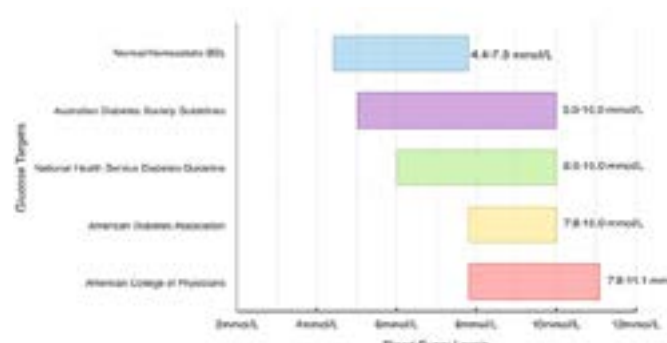


Figure 1. Recommended perioperative BSL targets

Current Recommendations

Given that studies have failed to show a benefit and some even show increased mortality with intensive insulin therapy, the management of glucose concentrations has undergone drastic changes in the past decade. Current recommendations from the UK, US, and Australia all recommend a similar range of blood glucose concentrations (Figure 1). Most guidelines tolerate mild hyperglycaemia as it reduces the potential for developing hypoglycaemia. Insulin therapy in both general medical and surgical settings should consist of a mixture of basal, prandial, and supplemental insulin (basal-bolus), instead of the sliding-scale regimen. However, differences in these recommendations indicate that the most optimal blood glucose concentrations are still unknown.

Preoperative insulin therapy should focus on obtaining good glycaemic control, while avoiding episodes of hypoglycaemia. The Endocrine Society's Clinical Guidelines recommend a fasting blood glucose concentration of <7.8 mmol/L and a random blood glucose concentration of <10.0 mmol/L for the majority of hospitalised patients with non-critical illness. [41] For avoidance of hypoglycaemia, therapy should be reassessed when blood glucose concentration falls below 5.6 mmol/L. Similarly, the National Health Service Diabetes Guideline published in 2012 by Dhatariya *et al.* recommends blood glucose concentrations between 6.0–10.0 mmol/L, while accepting 4.0–12.0 mmol/L. [42] The Australian Diabetes Society currently recommends a blood glucose target of 5.0–10.0 mmol/L in both the ICU and non-ICU settings. [43] The American Diabetes Association and the American Association of Clinical Endocrinologists currently recommend commencing insulin therapy for critically ill patients with persistent hyperglycaemia (>10.0 mmol/L), and to aim for a blood glucose target range between 7.8–10.0 mmol/L, [44] while the American College of Physicians recommends 7.8–11.1 mmol/L for critically ill patients. [45]

The mainstay of type 2 diabetes therapy is oral hypoglycaemic agents, such as metformin and sulfonylureas. Most guidelines suggest withholding oral anti-diabetic agents and non-insulin injectable medications on the day of surgery but not before. For major surgeries, metformin should be withheld for at least 24 hours. This is because

oral diabetic medications can potentially produce hypoglycaemia during the fasting period prior to surgery, as well as systemic effects that may affect postoperative outcomes. For example, sulfonylureas can interfere with the opening of cardiac KATP channels, which increases the risk for myocardial ischaemic injury. [46] Metformin can potentially induce lactic acidosis if renal function is impaired. [47] However, ceasing anti-diabetic therapy too early may compromise glucose control, hence short- or medium-duration insulin should be used to treat acute hyperglycaemia during the operative period. Oral hypoglycaemic agents should not be restarted until adequate and regular oral intake is resumed.

The majority of patients receiving insulin therapy should use a basal-bolus insulin schedule. The long-acting agents are aimed at providing a steady, basal level of insulin while the shorter-acting bolus insulin is used to counter acute increases in blood glucose. It is important to note that not only type 1 diabetics, but all insulin dependent patients, will require insulin perioperatively, despite their fasting status. This is because these patients are insulin deficient and require consistent basal insulin replacement to prevent unchecked gluconeogenesis and ketosis.

Conclusion

Hyperglycaemia has been shown to produce deleterious effects in

multiple body systems, both acutely and chronically. Studies indicate that adequate glycaemic control during the perioperative period is beneficial for both short-term and long-term surgical outcomes. While the optimal target blood glucose range is still unclear, the literature supports the use of moderately strict glycaemic control for the management of hyperglycaemia in surgical patients. The use of basal-bolus insulin is preferred over the more traditional sliding-scale insulin for its efficacy and safety. With the current trend of rising diabetes incidence in Australia, maintaining good glycaemic control during the perioperative period will become an increasingly important challenge faced by health professionals.

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Conflict of interest

None declared.

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Is cellular senescence a viable strategy and endpoint for oncological control?

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Kok-Ho's interest lies in infectious diseases and oncology as well as the application of novel theoretical concepts to the development of better cancer treatment strategies. His primary motivation in medicine is to find a novel therapy for cancers with poor prognosis so that patients who are incurable now may have a new lease of life in the near future.

Apoptosis is considered the main form of cell death in cancer cells undergoing cytotoxic treatments such as chemotherapy and radiotherapy. However, disappointing treatment response rates in some cancers have prompted a rethink regarding oncological control methods. Cellular senescence has emerged as a possible tumour suppression strategy that may effectively control cancer cells when apoptosis fails. Understanding the mechanistic workings of senescence in the context of cancer cells may shed light on its feasibility as a clinical strategy.

Introduction

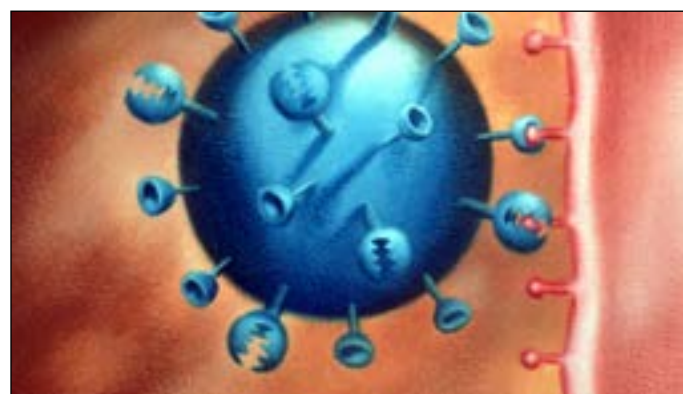
Conventional cancer therapeutics such as chemotherapy rely heavily on cytotoxicity to achieve maximal cell death. The rationale behind this approach is that elimination of cancer cells, and consequently tumour burden, will help achieve the best clinical outcome. Induction of cell death as an immediate clinical endpoint might be seen as an obvious choice, but it is worth contemplating whether this short-term benefit is incurred at the expense of long-lasting remissions. Many of the anti-cancer agents used in chemotherapy activate DNA damage signalling pathways which lead to apoptosis. However, apoptotic pathways tend to be defective in cancer cells. This could explain why response rates are sub-optimal despite aggressive regimens. The continued use of cytotoxic agents also promotes the development of resistant clones which can repopulate the primary tumour or metastasise to distal sites. If cell death is not always the best way to achieve sustainable cancer control, is there an alternative strategy or endpoint that overcomes the subversion of apoptotic cell death by tumour cells and is just as effective in blunting their proliferative nature?

One possible answer seems to be the induction of cellular senescence. Cellular senescence is classically defined as an irreversible state of growth arrest that occurs when cells encounter stress stimuli. Senescent cells are characterised by the following major features (Table 1).

Table 1. Major features of senescent cells.

Senescent markers	Altered morphology
1. Beta galactosidase at pH 6.0	1. Large and flattened cell
2. p16INK4a	2. Increased cytoplasmic granularity
3. Plasminogen activator protein 1	3. Increased number of vacuoles

Different forms of cellular senescence such as replicative (i.e. due to telomere shortening) or oncogene-induced senescence exist. Senescence-like phenotypes can be rapidly induced by genotoxic stress imposed by chemotherapy or radiotherapy, also known as accelerated cellular senescence (ACS). [1] Both apoptosis-competent and apoptosis-defective cancer cells may still be controlled by senescence, therefore implicating it as an important tumour-suppressive mechanism. [2] However, chemotherapy may not always provide durable responses as subsets of cancer cells are capable of escaping senescence and resuming cell division. The utility of senescence has, thus, remained inconclusive. This article will attempt to briefly explore the mechanistic insights of cellular senescence in cancer cells and assess its feasibility



as a clinical strategy or endpoint in oncological control.

Mechanistic insights into the role of cellular senescence in cancer cells

It was originally observed that cells that undergo senescence often do not divide even in the presence of mitogenic stimuli. Genomic stress from the environment can induce DNA damage pathways which inhibit cell cycle progression. In cancer cells, two important pathways are the p53 and p16INK4a/pRB pathways. [2] p53, p16INK4a, and pRB are important tumour suppressor proteins. While the mechanisms are still unclear and the contributions of p53 and p16INK4a may differ in different cancer cell types, it is suggested that p53 may be important for the establishment of senescence while p16INK4a maintains it (Figure 1). [3,4]

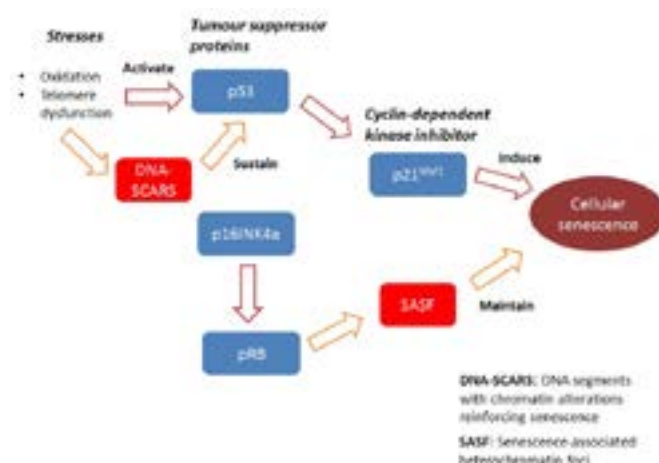


Figure 1. Role of p53 and p16INK4a/pRB in cellular senescence.

Activation of p53 by stresses such as oxidation and telomere dysfunction lead to upregulation of the cyclin-dependent kinase (CDK) inhibitor p21^{Waf1} which, in addition to apoptosis, causes cell cycle arrest and senescence. The activity of p53 is sustained by stress-induced DNA damage response signals which come from DNA damage foci, also known as DNA segments with chromatin alterations reinforcing senescence (DNA-SCARS). On the other hand, p16INK4a is essential for maintenance of senescence via the activation of the retinoblastoma (pRB) tumour suppressor protein. The pRB protein helps form senescence-associated heterochromatin foci (SAHF) which can silence tumour-promoting genes. [4]

Cancer cells can be cleared by apoptotic cell death, however, those which are resistant to initial apoptosis may be diverted to alternate pathways such as senescence, where they face a number of possible outcomes. [5] Firstly, cancer cells that undergo senescence are still capable of being eliminated by apoptosis at a later time. Secondly, senescent cancer cells may go into a terminal proliferative arrest state. It has been suggested that there is significant cross-talk between terminally arrested cancer cells and the immune system. Prolonged terminal arrest can trigger the clearance of cancer cells via phagocytosis and immunogenic cell death by autophagy. [6] Alternatively, immune mediators such as cytokines may be required for the maintenance of terminal arrest. [7] Dysregulation of this cross-talk can potentially result in bypass of cellular senescence and escape of cancer cells. The second outcome is interesting in a therapeutic sense as the involvement of immunogenic cell death is likely to bring about more sustained control than apoptosis. Apoptosis generally does not trigger an inflammatory response and the fact that cancer cells may harbor apoptotic defects suggests that this method of tumour suppression is not efficient. In fact, there is recent evidence that apoptosis may not even be the predominant mode of cell death in most cells, implying that other modes of cell death should be considered in cancer therapy. [8]

Senescence-associated secretory phenotype

While senescent cells exist in a state of growth arrest, they are still metabolically active and secrete a number of cytokines, chemokines, growth factors, and proteases which have important tumour-suppressive and tumour-promoting consequences. This unique phenotype is known as senescence-associated secretory phenotype (SASP) and can be found in senescent cells with DNA-SCARS. [9] As mentioned above, terminal arrest may be maintained by certain immune mediators. [4] These immune mediators may be secreted in an autocrine manner and help reinforce growth arrest. Examples of these tumour-suppressive mediators include plasminogen activator inhibitor-1 (PAI-1), and insulin-like growth factor binding protein-7 (IGFBP-7). On the other hand, tumour-promoting mediators can be secreted in a paracrine manner and induce aggressive phenotypes in neighbouring cells. These include factors such as matrix metalloproteinases (MMPs), amphiregulin, vascular endothelial growth factor (VEGF), as well as growth-related oncogene- α and β (GRO- α & GRO- β). [4]

Certain pro-inflammatory cytokines such as interleukin-6 and interleukin-8 (IL-6 and IL-8) have paradoxical effects on tumour progression and their exact role may depend on the immune contexture. Chronic low-level inflammation can promote tumour progression whereas an acute high-grade inflammatory response can result in tumour regression. [10] It is worth postulating that the stimulation of immunogenic cell death via the second outcome may actually assist in augmenting pro-inflammatory cytokine levels in the acute phase, leading to elimination of cancer cells. On the other hand, apoptosis does not promote adequate IL-6 and IL-8 levels to result in clearance of these cells. Instead, epithelial-to-mesenchymal transition and the cell migration/invasion effects of these cytokines may become dominant, resulting in metastatic phenotypes. Besides secreting chemokines to attract immune cells, senescent cells also express ligands for cytotoxic immune cells such as natural killer (NK) cells, allowing for immune-mediated clearance of cancer cells. [11] It would seem counterintuitive that cellular senescence can have tumour-suppressive and tumour-promoting effects at the same time. How then, can we reconcile these paradoxical effects?

A temporal model of senescence

Cellular senescence is not a phenomenon restricted to cancer cells. In fact, it is a highly conserved process also found in normal cell types such as fibroblasts, and is involved in tissue repair as well as age-related degeneration. [12] Many of the tumour-promoting secreted factors found in the SASP are actually required for tissue regeneration. For example, VEGF is involved in angiogenesis while MMPs are required for degrading of fibrotic tissues found in damaged tissues. [13] Similarly,

ageing tissues are characterised by low levels of chronic inflammation which can be mediated by factors such as IL-6 and IL-8. [14] The SASP is therefore a changing entity which differs in its secretory repertoire depending on the context it is expressed in. Rodier and Campisi proposed a model in which the senescent phenotype can be organised temporally. [15] In this model, the senescent phenotype increases in complexity with time. The initiating event is an oncogenic stress which either results in immediate repair and recovery of cells or induction of senescence. Once senescence occurs, cells are terminally arrested, resulting in tumour suppression. The SASP is then activated and IL-1 α is secreted. This cytokine binds to the IL-1 receptor and induces a signalling cascade which leads to the activation of transcription factors such as NF- κ B and C/EBP β . This in turn stimulates SASP factors such as IL-6, IL-8, and matrix metalloproteinases (MMPs) which are involved in both tissue repair and tumour progression. At the same time, pro-inflammatory cytokines such as IL-6 and IL-8 may increase to such high levels that they feed back and reinforce tumour suppression.

In addition, senescent cells may express a number of cell surface ligands and adhesion molecules which attract immune cells and result in clearance. During the later stages of senescence, the SASP phenotype is tuned down through the expression of microRNAs such as miR-146a and miR-146b so as to prevent the persistence of an acute inflammatory response. [16] However, the consequence is a chronic inflammatory state which can be perpetuated by imperfect immune clearance. A small number of senescent cells persist and contribute to chronic inflammation via their pro-inflammatory cytokines, which can eventually lead to the formation of an ageing phenotype. This phenotype is characterised by impaired functionality and increased vulnerability to cell death. It is apparent from this model that there is a delicate balance between different SASP phenotypes and imperfect immune processes can easily tilt the balance towards detrimental outcomes such as tumour progression and ageing phenotypes.

Susceptibility to tumour progression is not unexpected considering that important tumour suppressive proteins such as p53 and p16INK4a are often deficient or defective in cancer cells. [17] Although the defects in p53 and/or p16INK4a can be hurdles, these 'weaknesses' also provide unique opportunities for therapeutic interventions. In fact, cellular senescence might have originated foremost as a beneficial biological response. From an evolutionary perspective, it is suggested that senescence could have evolved to promote tumour suppression and tissue repair in young organisms. [4] These activities were selected as they are necessary for organismal survival in early harsh environments. However, unselected activities such as tumour progression and aging still occur as survival to old age is rare in harsh environments, and therefore selection against these detrimental activities is weak and tends to decline with age. It is therefore quite likely that senescence was meant to be a major tumour-suppressive mechanism and not simply a 'backup' plan to the more widely recognised apoptotic cell death.

Cellular senescence as a clinical strategy

While cellular senescence was initially thought to be irreversible in normal cells, a few studies have suggested that this process is reversible in cancer cells under the right conditions. For example, studies focusing on the tumour suppressors p53, pRB, and p16 found that suppression of these proteins in fibroblasts led to the reversal of the senescent phenotype. [18] Similarly, lung cancer cells were able to escape senescence through the up-regulation of Cdc2/Cdk1 and subsequently increased production of survivin, a protein involved in cell resistance to chemotherapy drugs such as paclitaxel. [19] This potentially implicates senescent cells as a repository for re-emergence of carcinogenesis. However, it should be noted that there is a lack of evidence which suggests that cell-cycle re-entry is a sign of recovery of full proliferative capacity. Cells which re-enter the cell cycle may still be subjected to cell death by apoptosis or mitotic catastrophe at a later stage. [20]

In solid tumours, the use of chemotherapy alone yields a disease response rate of 20-40% and complete tumour eradication is often difficult to achieve. Considering that most anti-cancer agents kill by apoptotic cell death, this seems to suggest that apoptosis may be limited in its clinical efficacy. [21] Furthermore, regardless of whether cellular senescence is reversible or not, *in vivo* analysis of treatment responses in primary lymphomas have shown that senescence improves the outcome of cancer therapy despite the lack of intact apoptotic machinery. [17] One of many possible reasons for the improved outcome could be the prevention of cancer stem cells (i.e. precursor cancer cells) via the inhibition of mechanisms similar to induced pluripotent stem (iPS) cell (i.e. stem cells generated from adult tissue) reprogramming. [21] This is because potent inducers of senescence such as p53 and p16INK4a are also potent inhibitors of iPS reprogramming. There is also potential for senescence-based therapies to yield synergistic and additive treatment effects as conventional modalities such as chemotherapy and radiotherapy can induce ACS. [22] Therefore, attempts should be made to further consider senescence as a potential treatment strategy.

There are a number of possible directions that can be pursued in a senescence-based strategy. Firstly, the activity of tumour suppressor proteins and senescence-inducers such as p53 can be enhanced. This can be attained through p53 stabilisation or mutant p53 reactivation. p53 stabilisation was found to be mediated by small molecules known as nutlins. These molecules inhibit the E3 ubiquitin-protein ligase MDM2, which is a potent inhibitor of p53. Similarly, restoration of p53 was achieved by compounds such as the pro-apoptotic factor PRIMA-1^{MET} and DNA intercalator ellipticine, which induce structural changes in the mutant protein and promote transcription of p53 targets. [23,24] Another possible target could be the inhibition of cell cycle progression via CDK inhibitors. One of the first CDK inhibitors to be tested in clinical trials is flavopiridol, which has been shown to exert tumour-suppressive effects in a number of malignancies such as colon and prostate cancer. [25] Flavopiridol, in certain doses, also appears to enhance treatment response when used in conjunction with standard chemotherapy agents, illustrating the proof of concept that senescence can augment existing treatment modalities. More recently, studies have investigated the use of statins in patients after neoadjuvant chemotherapy. Statins were shown to down-regulate key cell cycle mediators such as Cdk1, cyclin B1, and survivin, and up-regulate the CDK inhibitor p27. [21] However, antagonistic effects were also observed when statins were administered alongside chemotherapy

due to escape from senescence. These observations suggest that the effects of statins need to be examined further, particularly in relation to their use before, during, or after chemotherapy. Besides modulation of p53 function and the use of CDK inhibitors, senescence can also be induced by inhibition of important oncogenes such as MYC. [26] MYC over-expression in tumours is associated with a poor prognosis when chemotherapy is used. By inhibiting MYC through small molecule inhibitors such as 10058-F5 and its derivatives, the expression of a number of genes involved in cell proliferation can be suppressed, contributing to cellular senescence. [27]

Conclusion

In summary, cellular senescence may be a viable strategy for oncological control. Although its therapeutic potential was first recognised through its ability to bring about permanent growth arrest of cancer cells, this viewpoint is too simplistic. Cellular senescence is in fact a dynamic process characterised by a SASP which evolves in complexity with time. The reversibility or irreversibility of cellular senescence depends on the immune context and delicate processes that regulate senescence (e.g. immune clearance and deficiency of tumour suppressive proteins). Although senescence is dependent on multiple factors, we should consider it as a major tumour-suppressive mechanism alongside apoptosis. During carcinogenesis, subversion of anti-tumour responses is commonplace and should not be perceived simply as weaknesses in a clinical strategy. This is illustrated by the observation that cancer cells that do not apoptose can still subsequently undergo apoptosis at a later stage or are subjected to more immunogenic forms of cell death like autophagy. Senescence can therefore function as a potent failsafe tumour-suppressive mechanism. On the contrary, therapeutic interventions should anticipate and augment existing barriers to tumour progression. In senescence, a number of possible solutions such as p53 enhancement, CDK inhibitors and oncogene inhibition provide reason for optimism and should be investigated further.

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Get inspired.

Perioperative pain management – should we pre-empt or prevent pain?

Dr. Lukman James Anderson
BMed

Luke was awarded the ANZCA Faculty of Pain Medicine Prize for this review completed as a final year medical student. His interests include critical care medicine, anaesthetics, pain medicine, rural/remote health and medical education. He has aspirations for a career in anaesthesia. Interests outside of medicine include football, writing and learning Indonesian.

Central sensitisation is the process whereby nociceptive inputs trigger increased excitability and synaptic efficiency of central nociceptive pathways, and is a key process in the development of chronic postoperative pain. Pre-emptive analgesia, whereby analgesia is given prior to surgical incision, has previously been advocated as a method of decreasing the process of central sensitisation and its clinical consequences – namely hyperalgesia, allodynia and chronic post-surgical pain (CPSP). A systematic review of pre-emptive analgesia has demonstrated positive studies existing only for the modalities of epidural analgesia, NSAIDs and local anaesthetic wound infiltration. [1]

A shift towards preventive analgesia has been advocated, a strategy in which analgesia is given for as long as the sensitising stimulus remains present. [2-6] This may include the preoperative, intraoperative and post-operative periods. Systematic reviews evaluating preventive analgesia have returned a greater proportion of favourable trials. In particular, NMDA antagonists have been shown to be promising in the preventive setting, and have been observed to decrease perioperative pain and post-operative analgesic consumption. [7]

The concept of pre-emptive analgesia, where the main focus is on the timing of the intervention with respect to incision, should be replaced with the broader approach of preventive analgesia. Appropriate analgesia should be provided for as long as a sensitising stimulus remains present. Further research should focus on determining the analgesic regimens that most effectively decrease the clinical consequences of central sensitisation, including hyperalgesia, allodynia and CPSP.



Central sensitisation

The surgical process produces nociceptive signals via several mechanisms, including skin incision, tissue damage and post-operative inflammation. Repeated afferent noxious signals at the level of the dorsal horn can induce neuronal hypersensitivity, mainly from alterations to glutamate receptors and ion channels. [4] Alterations at the dorsal horn include increased membrane excitability, greater synaptic efficiency and decreased activity of inhibitory interneurons. [10] This produces the clinical consequences of central sensitisation, namely hyperalgesia and allodynia. It may also lead to the development of chronic post-surgical pain (CPSP), which affects 10-50% of patients post-surgically, and is severe in 2-10% of these cases. [4]

While general anaesthesia attenuates the transmission of noxious afferent signals to the spinal cord, it does not completely block it. [3] Systemic opioids may similarly fail to provide sufficient blockade at the dorsal horn to prevent central sensitisation. Hence, while the patient is unconscious during the procedure, the stimuli necessary for central sensitisation persist, leading to increased post-surgical pain with greater analgesic consumption, and possibly increasing the chance of developing CPSP.

N-methyl-d-aspartate (NMDA) has been implicated as a key substance in the development of central sensitisation. [10] There has been increasing interest in the role of NMDA antagonists such as ketamine, dextromethorphan and magnesium as agents in providing preventive analgesia. Possible mechanisms include direct effects at the dorsal horn, and by reduction of the development of acute opioid tolerance. [7]

Search strategy

MEDLINE was searched through to June 2014 using the following search criteria: preventive OR pre-emptive OR preemptive AND analgesia. 1166 results were returned. Studies qualifying as level one evidence by NHMRC evidence hierarchy were included in the review (systematic reviews and meta-analyses). 1155 results were excluded from the review as they did not qualify as level one evidence. Eleven studies were identified for inclusion.

Clinical evidence – pre-emptive analgesia

Clinical studies evaluating pre-emptive analgesia have shared several methodological flaws. Most often, this is due to a misunderstanding in what constitutes pre-emptive analgesia, with many studies instituting direct analgesia instead. There is also difficulty in establishing a valid control group, as all study participants must receive post-operative

Background

The relationship between intra-operative tissue damage and the amplification of post-operative pain was first described by Crile almost a century ago, in a process now referred to as central sensitization. [2] The concept of pre-emptive analgesia was proposed as a means of decreasing changes occurring in nociceptive pathways, resulting in minimisation of post-operative pain and analgesic consumption, as well as a decreased incidence of CPSP. [8] This approach involves the administration of analgesia prior to surgical incision. While this has been shown to effectively decrease dorsal horn changes associated with central sensitisation, clinical evidence has been equivocal. [9]

More recently, preventive analgesia has been proposed as a more effective method of modulating central sensitisation. Preventive analgesia focuses on blocking any nociceptive signals arriving at the dorsal horn by providing analgesia for as long as sensitising stimuli persist. [4] Interventions may extend from the pre-operative period until final wound healing, and are not confined to the pre-incisional period as for the pre-emptive approach. Preventive analgesia is defined in Acute Pain Management: Scientific Evidence as the “persistence of analgesic treatment efficacy beyond its expected duration”. [9, p.13] This approach has been found to be a more effective strategy for decreasing post-operative pain and analgesic consumption than a strictly pre-emptive approach. [2,6,9] Perioperative pain management should emphasise continuous analgesia for as long as a noxious stimulus is present, rather than focus on the timing of an intervention.

analgesia for ethical reasons. The administration of post-operative analgesia may attenuate the central sensitisation that occurs secondary to post-surgical inflammation, thus biasing the control group towards favourable outcomes.

Moiniche, Kehlet and Dahl reviewed double-blind, randomised, controlled trials (RCTs) which evaluated pre-incisional versus post-incisional analgesia, and the effect on postoperative pain control. [11] No clinical benefit was observed across the 80 included studies, across a spectrum of analgesic modalities. One included trial, however, found a significant reduction in pain at 6-months post radical prostatectomy with pre-emptive epidural analgesia. [12] An update on this systematic review revealed 30 further randomised trials published in the period 2001-2004. [13] Six out of eight trials published in this period reported reduced analgesic consumption and post-operative pain with pre-emptive NSAIDs. The results from studies evaluating other modalities remained uniformly negative.

A meta-analysis by Ong *et al.* [1] however supports the use of epidural analgesia, local anaesthetic wound infiltration and NSAID administration in the pre-emptive context. This analysis included RCTs comparing preoperative and intraoperative interventions. Outcomes measured were pain intensity scores, supplemental analgesic consumption and time to first analgesic consumption.

The meta-analysis by Ong *et al.* included 66 studies, with data from 3261 patients. The most marked effect size when combining outcome measures was observed with pre-emptive epidural analgesia (effect size 0.38; 95% CI, 0.28-0.47; $p < 0.01$). Epidural analgesia produced a positive effect when the three outcome measures were considered individually.

For each of these outcome measures, an effect size was calculated in order to control for the variety of pain scales used across studies. The calculated effect size for each outcome was then combined to measure a single theoretical construct – termed ‘pain experience’. Where the effect size and confidence interval (CI) exceeded 0, the effect was deemed to be statistically significant. This differed to the approach by Moiniche *et al.*, where the scores from the differing pain scales were converted into a single visual analogue scale (VAS) score and combined, and may have contributed to the conflicting results between the studies.

Anaesthetic wound infiltration and NSAID administration also produced statistically significant differences in ‘pain experience’. When outcomes were considered individually, time to first analgesic request was increased and analgesic consumption was decreased, but no effect on post-operative pain scores was observed. A 2012 systematic review of pre-emptive ketorolac administration observed decreased post-operative opioid requirements, and noted one small study which demonstrated benefits in post-operative pain scores. [14]

This meta-analysis includes trials that have since been withdrawn from publication. These trials related to pre-emptive local anaesthetic wound infiltration and NSAID administration. A re-analysis of the data by Marret *et al.* concluded that the retraction of these trials did not significantly alter the results of the study. [15] The study has further been criticised for a lack of detail regarding the review process, and the exclusion of non-English trials leading to publication bias. [1]

Katz and McCartney performed a systematic review of RCTs evaluating both pre-emptive and preventive approaches to analgesia, published from April 2001 to April 2002. [6] Of the twelve pre-emptive studies identified, five demonstrated a positive effect. The scope of the review is limited by the short time period analysed, but is the first to evaluate both pre-emptive and preventive study designs.

Clinical evidence – preventive analgesia

15 studies evaluating the efficacy of preventive analgesia were identified by Katz and McCartney, nine of which were positive trials. [6] One of these positive trials, demonstrating pain reduction with

bone marrow injection of opioids, has since been withdrawn from publication due to academic fraud. [16] Four of six studies examining the use of NMDA antagonists revealed lower post-operative pain and decreased analgesic consumption in the intervention group. Preventive effects were also observed with the use of clonidine and local anaesthetics.

The authors suggest that the percentage of positive trials observed in the study underestimates the true efficacy of preventive analgesia. This is because two of the pre-emptive trials may have in fact demonstrated preventive analgesia, but there was insufficient data presented regarding duration of analgesic effect to determine whether or not this had occurred. Three of the negative preventive studies were criticised due to inadequate provision of analgesia, thus precluding any preventive analgesic effect from occurring.

The limited amount of studies included means that the conclusions regarding the efficacy of preventive analgesia drawn from the review are weakened significantly by the retraction of the positive study by Reuben *et al.* [17] However, the study was influential in producing a shift from a pre-emptive approach to a preventive approach, by directly comparing these approaches in a single review. The efficacy observed in trials evaluating the role of NMDA antagonists also renewed interest in the role of these agents.

McCartney, Sinha and Katz performed a systemic review of RCTs evaluating NMDA antagonists (ketamine, dextromethorphan or magnesium) in preventive analgesia. [7] The primary outcome was reduction in pain, analgesic consumption or both in a time period beyond five half-lives of the drug utilised. Ketamine was found to have a positive effect in 58% (14 of 24) of included studies, and dextromethorphan was positive in 67% (8 of 12). No preventive effects were observed in four studies of magnesium.

The effect of NMDA antagonists on the incidence of CPSP is unclear. Low-dose intravenous ketamine administered with thoracic epidural analgesia has been observed to confer reduced post-thoracotomy pain in the immediate post-operative period and at one and three months after surgery. [18] A more recent RCT, however, noted no difference between ketamine and normal saline at four months post-thoracotomy, although it did confer post-operative pain relief. [19] The conflicting results may have been influenced by the difference in post-operative pain management, with the positive study providing a continuous ketamine infusion 3 days post-operatively. In the setting of colonic resection, a study of multimodal intraoperative epidural analgesia (local anaesthetic, opioids, ketamine and clonidine) revealed a reduction in pain 1-year post operatively. [20]

Practice guidelines

The aforementioned areas of uncertainty and controversy regarding pre-emptive and preventive analgesia have hindered the development of any formal guidelines to guide clinical practice. The Australian and New Zealand College of Anaesthetists (ANZCA) position statement ‘Guidelines on Acute Pain Management’ states that “preventive treatment of postoperative pain may reduce the incidence of chronic pain”. [21,p1] The ANZCA publication ‘Acute Pain Management: Scientific Evidence’ presents several key messages, and outlines the efficacy of pre-emptive epidural analgesia, preventive NMDA antagonist administration and ketamine (in colonic surgery only), but does not provide specific clinical recommendations. [9]

Regardless of the controversies that surround the issue, effective post-operative and long-term pain management is fundamental to quality patient care. Post-operative pain control should be individualised and a management plan should be developed prior to surgery, in partnership with the patient, taking into account psychosocial factors that may influence the pain experience. This should be based upon a thorough history, taking into account prior pain experiences, past analgesic use, current medications and immediate patient concerns. [2] ANZCA recommends a multimodal approach, as to improve efficacy of each

drug, provide lower doses of individual drugs and reduce the risk of significant side effects. [21] Non-pharmacologic therapies should be instituted as a part of a multimodal approach where appropriate.

Conclusion

The process of central sensitisation has been the target of multiple methods of intervention in a wide array of treatment modalities, with the aim of decreasing post-operative pain, decreasing analgesic consumption and reducing the incidence of CPSP. The development of a meaningful evidence base has been encumbered by definitional confusion, difficulties with study design and academic misconduct leading to the retraction of articles. It is, however, apparent that the concept of pre-emptive analgesia should be replaced with the broader approach of preventive analgesia, and appropriate analgesia should be provided as long as a sensitising stimulus is present. Further research

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should focus on determining the analgesic regimens that most effectively decrease the clinical consequences of central sensitisation, including hyperalgesia, allodynia and CPSP.

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The impaired student: Substance abuse in medical students

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Substance use disorder has been a significant issue within the medical profession throughout history. It is recognised as an important issue of concern, particularly due to its associated mortality, morbidity and social consequences. Although a substantial body of literature addresses this issue amongst doctors, there is little discussion focusing on medical students. This review summarises the existing literature available on the epidemiology, common presenting features, management, legal implications and mandatory notification requirements of substance abuse in the medical student. Limited evidence suggests concerning levels of hazardous alcohol use exists in medical students, however alcohol and drug use is not comparatively higher than the general student population. While early detection is optimal for harm prevention, signs and symptoms of substance abuse are subtle and easily missed. Prevention and early intervention is critical, and it is important for students to recognise possible signs of substance abuse in their colleagues, as the biggest barrier to treatment is denial. Once detected, current evidence from Physicians Health Programs suggests a service to manage the student's multidisciplinary care, follow up and return to study obtains the best outcome. As a chronic medical condition that carries significant risk of harm to the impaired student – and potentially to patients – all health professionals should be aware of this issue and their mandatory reporting obligations.

Introduction

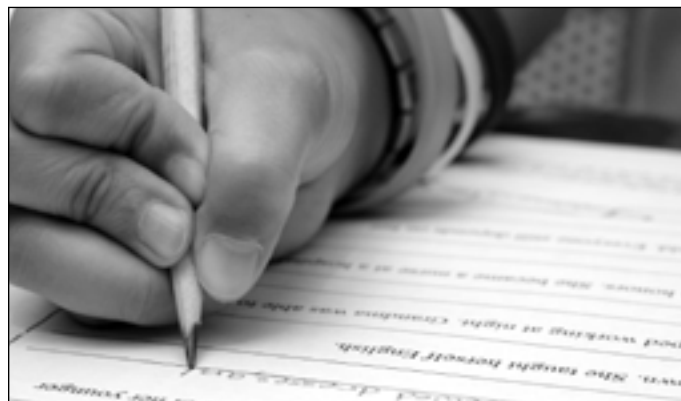
Substance use disorder (SUD) amongst doctors is an issue of significant concern. It is estimated the lifetime prevalence of substance abuse in Australian doctors is approximately 8%. [1] There is limited literature or discussion, however, addressing this issue in the context of the most junior members of the profession, medical students. The university experience is often coupled with alcohol use and occasionally with casual illicit drug use, but this is, to some extent, accepted, perhaps as part of youthful exuberance, experimentation or a rite of passage. [2] For some, however, this substance use may manifest as, or progress to, substance abuse: a pattern of drug or alcohol use that is detrimental both to the individual and to society. [3] For the substance-abusing medical student, there is a wide scope for serious implications personally, professionally and with the public.

This article aims to highlight the importance of this topic and provide information on the concept of substance use disorder, common signs of substance abuse, management, reporting requirements and legal implications. It also addresses why it is imperative there is awareness for this issue in medical students to prevent serious health consequences and risk to the public.

Terms within this article

Substance use disorder or substance abuse: A chronic condition characterised by a pathological pattern of behaviours related to substance use, manifesting as two or more symptoms of: impaired control of drug use; social impairment at work, school or home; risky use; tolerance or withdrawal. [4]

Substance dependence: An inability to control substance use, despite problems caused by use. [5] This may manifest physically or psychologically with tolerance or withdrawal. Dependence and drug



abuse are not separate entities within the Diagnostic and Statistical Manual 5 (DSM-5), however these terms are prevalent in the cited literature.

Impairment: A physical or mental impairment, disability, condition or disorder (including substance abuse or dependence) that detrimentally affects, or is likely to detrimentally affect, a practitioner's capacity to practise the profession. [6]

How common is student substance abuse?

There is little recent, comprehensive data on student substance abuse, with most studies occurring in the 1980s-1990s and concerning rates of use rather than abuse. [5] Furthermore, prevalence studies are hindered by surveys requiring self-reporting of abuse and varied case definitions. With these limitations, the available data on student substance use is summarised below.

Alcohol use and abuse

Use of alcohol in the general student population is common, with consumption occurring in approximately 96% of Australians aged 18-21 years. For medical students in particular, international studies have indicated that rates of lifetime alcohol usage range between 62.3% and 98.1%. [2,5,7-11] Male medical students have higher levels of intake compared to females and hazardous alcohol use is significantly higher in those with high levels of psychological distress. [12] The BeyondBlue study of medical students and doctors found concerning rates of moderate-risk (21%) and high-risk (4%) drinking amongst medical students in Australia. [12] Moderate risk is classed as a hazardous intake level and high risk is associated with harmful drinking patterns, as assessed by the World Health Organisation Alcohol Use Disorders Identification Test (AUDIT). [12] This level of drinking, however, appears low in comparison to the general university population, which has an approximately 8.1% rate of harmful drinking. [12,13]

Internationally, 50% of medical students in the UK consumed above the recommended amount. [8] Using the CAGE questionnaire (Table 1), 22.4% of junior Turkish medical students and 52.5% of Irish medical students were found to be CAGE positive. [10,11] Of medical students who drink, 60.5% of men and 72.2% of women engaged in binge drinking, with 36.8% of men and 58.2% of women suggesting that their performance had been affected at least one day in the past month by alcohol consumption. [8] While the BeyondBlue study noted that drinking levels decreased with age, other data suggests that as students progress through their clinical years and beyond, a greater

Table 1. The CAGE questionnaire. 'CAGE positive' is defined as two or more positive responses and indicates a high likelihood of problem drinking. [15,16]

1. Have you ever felt you needed to **C**ut down on your drinking?
2. Have people **A**nnoyed you by criticising your drinking?
3. Have you ever felt **G**uilty about drinking?
4. Have you ever felt you needed a drink first thing in the morning (**E**ye-opener) to steady your nerves or to get rid of a hangover?

number of students drink, and drink more heavily. [10,14]

Drug use

Rates of illicit substance abuse in medical students appear comparable to, or less than that of, the general population, with data falling between 3-10%. [17] BeyondBlue reports show low rates, with 10.2% of students engaged in illicit drug use 2-3 times a month, and 0.5% 1-6 times a week. [12]

Drugs of abuse may be recreational, for example cannabis or stimulants, or prescription, such as benzodiazepines, opiates or propofol. Amongst junior students, the most common drug of abuse is cannabis and is often likely to be the first used before medical school. [2,8,14] Other illicit or prescription drugs are less common, however alcohol and cannabis might be considered gateway drugs to these. In one study, those who used cannabis were more likely to be drinking heavily than non-users and those who used illicit drugs had also used cannabis. [14] It is reported that medical students are increasingly being offered illicit drugs, and more are accepting them. [11] Abuse of illicit drugs, such as cocaine, or prescription drugs, such as benzodiazepines, was more likely to occur once at university. [2]

Notably, as students progress to become doctors, patterns of drug abuse change with increasing rates of prescription drug abuse. [5,10] Drugs of choice vary by medical specialty as to what is easiest to obtain; for example, anaesthetists have high rates of propofol and opiate abuse, whereas other specialties such as psychiatrists are more likely to abuse benzodiazepines. [1,18,19].

Recognition of substance abuse

Signs of substance abuse are both subtle and varied, and can be easily missed. They are often disguised by the affected practitioner. Denial is common, and often it is the person with the disorder that is last to acknowledge a problem. [20] Early detection can prevent the development of significant harm. Table 2 lists possible emotional, social and physical signs of alcohol or drug abuse.

Reporting requirements

The impaired physician is a concept defined under national law as a physical or mental impairment, disability, condition or disorder (including substance abuse or dependence) that detrimentally affects, or is likely to detrimentally affect, a practitioner's capacity to practise the profession. [6] For a student, the impairment must detrimentally affect, or be likely to detrimentally affect, the student's capacity to undertake clinical training. This means impairment is defined by a student's reduced capacity to learn, a quite broad definition. For a notification to the Australian Health Practitioner Regulation Agency (AHPRA) to be made, however, there must be a belief that their impairment could cause public harm, for instance intoxication at work. [6,23]

Two forms of notification can be made to AHPRA. [6] Mandatory notifications compel practitioners or education providers to make a notification if they form a reasonable belief that a student has an impairment that may place the public at substantial risk of harm in the course of their clinical training, or are practising whilst intoxicated with alcohol or drugs. Voluntary notifications about a student can be made by anyone if they form a reasonable belief that a student has an impairment that may cause public harm.

Consequences of notification may include the suspension of a

Table 2. Possible emotional, social and physical signs of alcohol or drug abuse. [5,20-22]

Emotional	Social	Physical
Personality change	Behavioural change	Dishevelled appearance
Mood swings/anxiety	Erratic or decreased performance	Weight loss
Irritability	Drunk/intoxicated often at social events	Change in diet
	Social withdrawal	Smell of alcohol
	Lateness	Unexplained minor injuries
	Relationship problems	Signs of intoxication or withdrawal e.g.
	Problems with law enforcement	slurred speech,
	Sexual promiscuity	tremors, excessive sweating, dilated
	Patient complaints performance	or pin point pupils
	Drunk/intoxicated often at social events	Needle marks
	Social withdrawal	Addition of long sleeves
	Lateness	
	Relationship problems	
	Problems with law enforcement	
	Sexual promiscuity	
	Patient complaints	

student's registration, the imposition of conditions of practice, further health assessment, and possible long-term impacts on their ability to continue their studies and future registration (depending on expert advice in each case). [6,23] For students, it is important to recognise the possible future career consequences of alcohol or drug abuse.

Management of the impaired student

Treatment of impairment is both complex and individualised and there is no standard protocol for treating impaired medical students. Treatment may be managed by the student and their treating team, or may be arranged by AHPRA or the medical board as a result of a notification. Individual medical school impairment policies likely vary and are not reviewed here. A majority of reviewed American school policies require direct referrals for management of suspected substance abuse cases, and one third forego disciplinary treatment for those impaired students who self-refer to promote seeking early intervention. [5] Depending on the substance(s) involved, treatment may include features such as inpatient treatment and detoxification, 12 step programs or use of therapeutic agents (e.g. naltrexone). [3]

Referral to a long-term support program with a specific focus on doctors' health is optimal. Within Australia, available services and models of support vary from state to state. Most states offer a Doctor's Health Advisory Service telephone counselling service, with support offered by experienced practitioners. [24] The Victorian Doctors' Health Program (VDHP) offers the only full-time physician health program (PHP) of its kind in Australia. It is confidential, independent of AHPRA and open to both doctors and medical students. [25] PHPs were pioneered in the United States to assist in the rehabilitation of impaired physicians. They do not directly provide treatment but provide evaluation and diagnosis, facilitation of formal addiction treatment, on-going confidential support, case management, biochemical and workplace monitoring, and return-to-work support as required on a case-by-case basis. [25,26] A core component is an individualised care contract lasting up to five years to ensure compliance with the appropriate treatment plan devised. This may include a case manager, psychiatrist, addiction specialist, psychologist, general practitioner or social worker. Ongoing peer support is also recommended through a facilitated Caduceus collegial support group open to medical practitioners and students with substance abuse issues, and has been shown to play an important role in recovery. [1] The VDHP offers three

types of programs of different levels of support, ranging from intensive case management to wellbeing and support programs and long term follow up, depending on what is required in each case and the phase of recovery. These programs are successful, with studies consistently demonstrating success rates of 75-90% after five years for American physicians treated through PHPs. [27,28] Preliminary data from the VDHP program indicates similar Australian five-year success rates. [25]

The evidence-based success of these programs suggests that similar services should be available for all doctors. However, cost is a significant issue. The average American state PHP costs USD\$521,000 annually to manage between 65 to 75 physicians per year, primarily paid for by an additional \$23 charge to licensing fees, whilst formal treatment costs are covered by health insurance and personal physician contributions. [27] It is important to note that some PHPs produce better outcomes than others and that implementation should replicate published successful models and be followed with outcome evaluations. [29,30]

Further to specific services available to doctors, there is a wealth of support available through the pastoral support and wellbeing services of universities that can be accessed in a student capacity. One proactive university even developed and successfully implemented an Aid for the Impaired Medical Student program to oversee medical student recovery management, although little has been published on this recently. [31]

Fighting the "conspiracy of silence"

Boisaubin and Levine discuss the concept of a "conspiracy of silence" where the impaired physician, his/her colleagues, friends and family have a tendency to dismiss their suspicions and suppress their concerns, with a belief that the physician is fine, or capable of solving his/her issues. [32] They state "denial is the most consistent hallmark of this disease process, for both colleagues and the susceptible physician." This is a key barrier to treatment, and only increases with professional advancement in a medical culture of not admitting weakness, let alone acknowledging the presence of a medical condition laden with stigma. Participants in the VDHP substance use programs were most likely to have been referred by colleagues, employers or treating doctors, compared to self-referral or referral from regulatory bodies. [1] This demonstrates the importance of students and educators being aware of the signs of substance abuse in others, and knowing the options available to assist.

Future implications

There is little data about the risks of student substance abuse, but death or near fatal overdose is the presenting symptom in 7-18% of doctors. [33] Alarmingly, recent data demonstrates anaesthetists abusing propofol have a 45% mortality rate. [19] Substance abuse is also often coupled with psychiatric morbidity and stress-related disorders. Harm to patients is a real risk, either indirectly through impairment of capacity and decision making, or directly, such as in the well-publicised case of the fentanyl-abusing doctor spreading Hepatitis

C to women undergoing pregnancy terminations. [34]

There is no clear longitudinal data to demonstrate whether substance abuse as a student is associated with substance abuse as a doctor. This article does not enter the debate as to whether impairment due to substance abuse as a student should preclude a student pursuing a career intimately associated with a range of drugs of abuse, such as opiates. Without prescribing rights, students are more limited in their access to the wide range of substances, compared with their qualified colleagues. It was noted that, of those surveyed in an evaluation of the VDHP Caduceus program, substance abuse issues began in medical school for 16% of the respondents. [1] Furthermore, the diagnosis of alcohol abuse is commonly delayed, often for years, and can start with patterns of high risk drinking.

Conclusion

In conclusion, substance use disorder has enormous impacts, including health issues, patient risk, mandatory notification requirements, future career implications and ultimately escalation to more dangerous substances. It is a chronic medical condition and management requires a multidisciplinary team, long-term support, sensitivity and experience. It is important to recognise that, while medical students are often high functioning and high achieving and generally appear to have similar rates of substance use to the general university population, they are not immune to substance abuse issues. In a profession with high levels of psychological distress, burnout and minor psychiatric morbidity, it is necessary to have a higher index of suspicion. [12] The biggest barrier to treatment is denial, not only by the impaired student, but also by friends, family and colleagues. It would therefore seem imperative that student substance abuse is detected early and treatment provided immediately to prevent the serious consequences of ignoring the situation.

If this article raises concerns for you or anyone you know, information on your local state service can be accessed at the Australasian Doctors' Health Network website <http://www.adhn.org.au/>. Crisis support is available 24hrs/day from Lifeline Australia on 13 11 14.

For useful general wellbeing information focused on medical students, Keeping Your Grass Greener is a fantastic guide available from the Australian Medical Student Association at: <https://www.amsa.org.au/initiatives/community-and-wellbeing/keeping-your-grass-greener/>

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Conflict of interest

None declared.

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Cannabinoid Hyperemesis Syndrome: A clinical discussion

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Amraj is a fifth year medical student with strong interests in general and emergency medicine.

This report describes a case of a 33-year-old female with cyclical vomiting associated with cannabis use, which was subsequently diagnosed as Cannabinoid Hyperemesis Syndrome (CHS). While the exact epidemiology of CHS is unknown, cannabis is the most commonly used illicit substance in Australia and the world.

CHS is typically characterised by the triad of heavy cannabis use, severe nausea and vomiting, and compulsive hot water bathing. The peculiarity of this condition lies in two specific associations: the link between cannabis and hyperemesis, as cannabis is usually known for its antiemetic properties, as well as the association with hot water bathing.

The following will describe a clinical case of CHS with a subsequent discussion on its pathophysiology, work-up, management, and a review of the current literature. It will also discuss how a multidisciplinary approach can be utilised to manage both medical and social aspects of this diagnosis.



Case introduction

Ms AB, a 33-year old female, presented to the Emergency Department with abdominal pain, nausea, and vomiting over the previous ten hours on a background of several years of cannabis and alcohol abuse. Her pain was generalised, dull, and had no particular aggravating or relieving factors. Her vomiting occurred every 20 minutes with no haematemesis, and there was no associated relief of her abdominal pain. Her last bowel movement was soft and twelve hours prior to admission, and there was no haematochezia or melaena.

Similar episodes of vomiting and abdominal pain have occurred several times over the past three years, with each prior episode lasting four to five hours and usually the day after abstinence from consuming cannabis. AB has found that taking hot showers multiple times a day provided her relief from her symptoms.

She last consumed cannabis and alcohol the day prior to admission. AB has consumed cannabis for the past 19 years (0.5 grams, 20 times a day), alcohol for the past twelve years (one bottle of spirits per day - approximately 20 standard drinks) and cigarettes (ten per day) for the past six years. AB is also a former intravenous (IV) drug user, however ceased 16 years ago after being diagnosed with hepatitis C. Her only other significant medical history is depression since 2005, for which she is prescribed 100mg of sertraline; however admits to taking this infrequently. She has never been pregnant and her last menstrual period was seven days ago.

Family history revealed a history of alcohol, drug abuse and mental health disorders in several first and second-degree relatives including her mother and father. She lives alone in Townsville and has had several failed rehabilitation admissions over the last few years. Systems review was unremarkable.

Examination

On admission, AB patient was agitated and distressed; however, was orientated to time, place and person.

Her hands were warm and sweaty with a capillary refill time of less than two seconds. There was conjunctival pallor. There was no jaundice, Osler's nodes, Janeway lesions, track marks, cyanosis or peripheral oedema. Four spider naevi were noted on the anterior chest wall.

Pulse	120bpm, regular
Respiratory rate	20 b/min
Blood pressure	180/115mmHg, right arm sitting
Temperature	36.3 degrees Celsius
Oxygen saturation	97% on room air
Glasgow coma scale	15/15
Body mass index	19kg/m2

Table 1. AB's vital signs in Emergency Department (ED).

Investigation	Remarkable Results
Urea & electrolytes	Normal; normal renal function
Liver function test	Gamma-glutamyltransferase: 262 iu/L Aspartate aminotransferase: 248 iu/L Alanine transaminase: 108 iu/L
Serum ethanol	55 mmol/L = 0.25% blood alcohol
Serum lipase	Normal
Electrocardiogram	Sinus tachycardia
Urinalysis / toxicology	Positive for cannabis, alcohol
Beta-human chorionic gonadotropin	Negative
Chest & Abdominal X-ray	Unremarkable

Table 2. AB's investigations in the Emergency Department.

There was no lymphadenopathy.

Her abdomen was mildly distended with generalised tenderness and a positive Carnett's sign. There was no guarding or rebound tenderness present. There were no masses or organomegaly and bowel sounds were present. Examination of her cardiovascular system revealed dual

heart sounds with no added sounds and her jugular venous pressure was not elevated. Her chest was clear on auscultation. Neurological examination was unremarkable.

Progress

Basic investigations were carried out as per Table 2. A hepatitis C viral load, liver ultrasound and biopsy, and upper endoscopy were also indicated to rule out acute causes, however, were not performed.

In ED, AB was given IV fluids, electrolytes, analgesia (paracetamol), thiamine, ondansetron (3 x 0.15 mg/kg doses) and metoclopramide (10mgIV) for her vomiting, and diazepam (20mg PO) for her withdrawal symptoms. Upon ward admission, she was also administered deep vein thrombosis prophylaxis.

On the ward, AB took up to ten hot showers a day, which she claimed helped with her symptoms. Due to her cyclical vomiting and history of past episodes, CHS was diagnosed. After being admitted for six days, liaising with the social worker led to AB's discharge directly to a community-based drugs and alcohol rehabilitation clinic.

Discussion

Incidence

Cannabis remains one of the most widely used illicit substances in Australia, with approximately one-third of Australians having tried it at least once in their life and one-tenth in the past year. [1] CHS was first described by Allen et al. in Adelaide, South Australia in 2004. [2] There are currently no epidemiological data on the incidence or prevalence of CHS among regular cannabis users. [3]

Clinical features of CHS

The diagnosis of CHS is made clinically based on the characteristic features. There are no diagnostic tests for confirmation of this disease. Therefore, very careful attention should be made to exclude more common and serious disorders first.

CHS is a cyclical disorder separated by symptom-free periods, which can be broken down into three phases: prodromal, hyperemesis and recovery. The triad of cardinal features include: [4]

1. Heavy cannabis use;
2. Recurrent episodes of severe nausea, vomiting, and abdominal cramping; and
3. Compulsive hot-water bathing for transient symptom relief

Emesis occurring in CHS starts profusely without prior warning, and is usually associated with symptoms such as nausea, sweating, colicky abdominal pain from retching, and positive Carnett's sign. [5] Further symptoms include sleeping difficulty, decreased appetite, weight loss, irritability, restlessness and increased anger and aggression. [4]

The most peculiar clinical feature is the compulsive bathing. It is so consistent amongst cases that multiple studies [3-7] have given it pathognomonic status for CHS. [3] It is not part of any psychosis or obsessive compulsion; rather, it is a form of learned behaviour, which becomes a compulsion once established in order to provide relief from severe nausea, vomiting and abdominal pain. [7]

The recovery phase can last from days to weeks and involves the person returning to relative wellness and normal bathing patterns. [6]

Pathophysiology

Cannabis has traditionally been associated with an antiemetic effect, which is why the concept of linking its abuse to hyperemesis seems paradoxical. Cannabis contains over 60 different cannabinoid substances, so without detailed research into all of these, it will be difficult to formulate an agreed-upon pathophysiology. [2]

From what is known, cannabinoids act on two types of cannabinoid receptors, CB1 and CB2. These are G-protein coupled receptors and inhibit adenylyl cyclase. [8] The three main types of exogenous cannabinoids found in cannabis include Δ^9 -tetrahydrocannabinol

(THC), cannabidiol (CBD) and cannabigerol (CBG). [8]

At low doses, THC is thought to exert an antiemetic effect centrally, by activating CB1 receptors in the dorsal vagal complex of the brainstem, [6] with the CBD and CBG appearing to further potentiate this. However, animal models show that higher levels, in fact, enhance vomiting. [9]

This, in combination with THC having high lipophilicity, could lengthen its half-life causing toxic concentrations, in addition to its ability to delay gastric emptying and dysregulate the limbic system. [2,9] The peripheral effects of cannabis could then override the central mediated antiemetic effect, causing hyperemesis.

The physiology behind CHS's most peculiar clinical finding, hot showering, requires more research. The hypothalamus is given much of the focus here, with subjective sensations initiating the need for a hot shower. There is debate between whether the body's core temperature plays a role. One proposition is the behaviour is due to the hypothermic effect by THC on the body's core temperature, whereas the other says it may be directly related to CB1 receptor activation. [10] Another theory is that the hot water causes a redistribution of the blood flow from the splanchnic circulation via the phenomena 'cutaneous steal syndrome', which then reduces stimulation of CB1 receptors in the gut bringing the patient temporary relief. [9]

All of these findings could be underlined by the proposition of Simonetto et al. that perhaps some patients may have a genetic polymorphism in cytochrome P450 enzymes responsible for cannabinoid metabolism, as it is uncertain why so few patients develop CHS despite the large prevalence of cannabis use. [11]

Differentials

Differentials for recurrent vomiting aside from CHS may include [4,7,9]:

- Cyclical vomiting syndrome (CVS)
- Psychogenic vomiting
- Abdominal migraine
- Hyperemesis gravidarum
- Gastrointestinal and pancreaticobiliary disorders e.g., pancreatitis
- Central nervous system disease
 - Tumour
 - Elevated intracranial pressure

A very common misdiagnosis of CHS is CVS; however, multiple features such as depression, anxiety and family history of migraines are typically negative findings of CHS, thus distinguishing the two. [6]

Workup, investigations and management

Management of CHS should be a multi-faceted approach starting in the emergency department. Firstly, one should complete a basic history, examination and work-up with the intent of ruling out common and life-threatening causes of acute nausea and vomiting.

Should it be warranted, unexplained vomiting and nausea could spark investigation for cannabis use. Normalising and asking questions without a negative tone is imperative to receiving honest answers. Sullivan [5] recommends asking, "have you ever tried marijuana for vomiting?" as well as "have you ever tried a hot bath or shower?" in order to gauge the likelihood for chronic cannabis use. In addition, one should ask the patient if they use synthetic cannabinoids as they can also cause CHS without showing up on immunoassay based urine drug tests. Synthetic cannabinoids are "designer drugs" constituent of alternative cannabinoids that produce similar pharmacological effects to cannabis by binding to the same cannabinoid receptors. Another limitation of immunoassay urine screening is despite it having 'good sensitivity and specificity for THC', [12] false positives can occur through cross reactivity with common drugs such as antoprazole and ibuprofen, passive inhalation of smoked cannabis as well as the use of hemp seed oil, which is why they should not dictate management in isolation. [13]



Figure 1. A general consensus amongst physicians for the management of CHS. 5-HT₃: Serotonin receptor; D₂: Dopamine receptor; H₁: Histamine receptor

Laboratory investigations are usually normal with few remarkable findings including mild leukocytosis, hypokalaemia, hypochloreaemia, and elevated salivary amylase. Nonetheless, investigations outlined in Table 2 would be appropriate for initial workup of vomiting presenting in the ED. In some cases, haematemesis may indicate an upper endoscopy and neurological findings may indicate brain imaging. [6]

From a medical point of view, the following management approach in Figure 1 is a general consensus amongst physicians for CHS as the focus is on intravenous fluids and supportive care due to there being no clear recommended pharmacological treatment. [5-7,14,15]

Analysis of management

Limited data exists for specific management of CHS, as it can only be speculated that by treating cannabis withdrawal, CHS can also be avoided. This is why supportive therapy is the major focus for CHS with a specific emphasis on anti-emesis. Due to both gastrointestinal and centrally located receptors being involved, 5-HT₃ receptor antagonists (most commonly ondansetron) and D₂ receptor antagonists (metoclopramide) are utilised. However, these drugs are largely ineffective in CHS with studies showing little to no improvement in patients. [2] Recent animal studies have demonstrated that haloperidol has great potential as an anti-emetic due to intricate interactions between dopamine and CB₁ signalling mechanisms. [16]

Dronabinol (synthetic THC) and rimonabant are drugs specific to managing cannabis withdrawal. A randomised, double-blind placebo-controlled trial by Levin et al. showed dronabinol to significantly lower withdrawal symptoms compared to placebo. [16] This is further supported by a study done by Haney et al. where withdrawal symptoms were also reduced. [17]

A study done on monkeys by Goldberg et al. found that dispensing rimonabant markedly reduced self-administration of cannabis but had no effect on self-administration of cocaine. [18] This is supported by findings by Huestis et al. where rimonabant blocked effects of smoked cannabis in human research volunteers, hence highlighting the

potential for rimonabant for cannabis dependency, which could then prevent CHS from occurring. It was also seemed to be well tolerated and the only major side-effect being mild nausea. [19]

One of the most recent proposals to management involves activating TRPV1 receptors, which are found in the peripheries. Such receptors can be activated by heat greater than 42°C or capsaicin. Lapoint, as reported by Gussow, [20] proposes it is the heat activation of TRPV1 that resolves symptoms, with seven cases being treated successfully via the use of topical capsaicin to the abdomen.

In addition to the pharmacological aspect, social management of cannabis use is also important, as randomised-controlled trials have shown techniques such as single session motivational interviewing as well as cognitive behavioural therapy being very effective in cannabis use cessation and maintaining abstinence. [15]

Conclusion

The diagnosis of CHS is made clinically after careful consideration of more common illnesses. The three characteristic features of CHS include heavy cannabis use, recurrent vomiting and compulsive hot water bathing. The treatment is largely supportive. Much of the pathophysiology and management is poorly understood and further investigation is warranted.

Consent declaration

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

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Conflict of interest

None declared.

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A case of haemorrhagic pericardial tamponade in an adolescent

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Pericardial effusions are not uncommonly encountered, and can be of infections, autoimmune, malignant and idiopathic aetiology. Large pericardial effusions may result in cardiac tamponade, which is a medical emergency. We report a case of a massive haemorrhagic pericardial effusion complicated by tamponade in a nineteen year old chef apprentice. He underwent an emergency pericardiocentesis, and made a quick recovery with symptomatic management. Upon follow-up, there was no recurrence of his effusion, and after extensive analyses of the fluid, no clear aetiology could be determined. Idiopathic pericardial effusions often pose a management challenge due to the difficulty of predicting the natural course and risk of recurrence.

Introduction

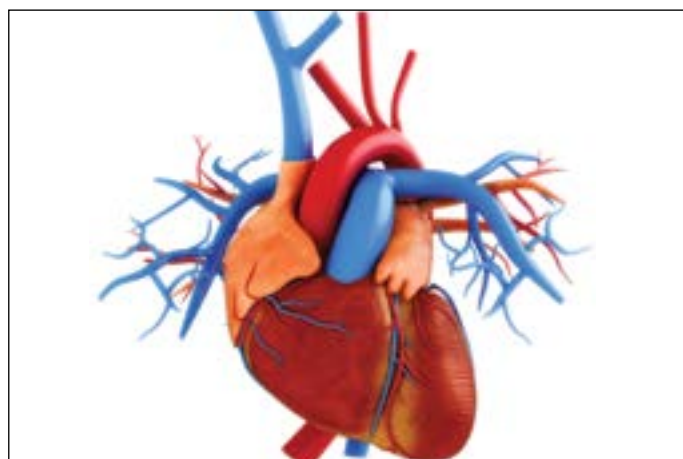
Pericardial effusion is the presence of excessive and sometimes abnormal composition of fluid in the pericardial space. Conditions that injure or insult the pericardium may lead to a pericardial effusion. In up to 60% of cases, it is associated with an identified or suspected underlying process and often linked with inflammation of the pericardium. [1] Nevertheless, in many cases, the underlying cause cannot be identified after extensive evaluation. Management of these idiopathic cases is more difficult due to their less predictable clinical course. To complicate the management, the patient in this case has haemorrhagic pericardial tamponade. Malignancy and tuberculosis are causes of haemorrhagic pericardial effusion that must be ruled out.

The Case

A 19 year old male, working as a chef apprentice, presented to the emergency department with acute onset of pleuritic chest pain and a two week history of progressive shortness of breath. The pain was characteristically sharp, central and aggravated on inspiration and supine position. He was systemically unwell with chills and night sweats. There were no prodromal respiratory tract symptoms, palpitations, syncope, cough, sputum and wheeze. He was otherwise healthy. He denied engaging in any high risk behaviour, any sick contacts or travel to the tropics.

On physical examination, temperature was 37.7°C, respiratory rate 20 breaths/minute, heart rate 114 beats/minute and BP 136/78mmHg. Oxygen saturation was 94% on 3L of oxygen. Cardiovascular examination was remarkable for distended neck veins, pulsus paradoxus of up to 20 mmHg and muffled heart sounds on auscultation. He had normal vesicular breath sounds over all lung fields. There was no lymphadenopathy or palpable masses to suggest malignancies, and no localizing signs to suggest a focus of infection.

An emergency echocardiography demonstrated a large pericardial effusion with right atrial and ventricular diastolic collapse, suggestive of cardiac tamponade. His chest X-ray revealed an enlarged cardiac silhouette and a small right pleural effusion.



An urgent pericardiocentesis was performed and 600mL of haemorrhagic fluid was drained through a pig tail catheter, with instantaneous improvement of his symptoms. Fluid analysis was consistent with an exudative effusion as determined by Light's criteria. However, focused evaluation for infective aetiology including viral serologies, serology for atypical organisms and mycobacterium were negative. No malignant cells were identified in the fluid. Table 1 reflects the extensive evaluation that was performed.

After a 48-hour period, his drain was removed. He was discharged home with a 6-week course of indomethacin for the intermittent pleuritic pain that persisted for a further two weeks with pantoprazole for gastroprotection. Upon subsequent follow-up a week later, there was no recurrence of his effusion with full resolution of symptoms. The repeat echocardiography performed a month later was normal.

Discussion

Recognizing pericardial tamponade

The pericardial space can hold approximately 15-50 mL of fluid under normal circumstances. The pericardial fluid acts as a lubricant between the parietal and visceral layers of the pericardium. This fluid is believed to be an ultrafiltrate of the plasma produced by the visceral pericardium. When significant amount of pericardial fluid accumulates, it develops into pericardial effusions. Large effusions may contain greater than 2 litres of fluid. [2]

Pericardial effusions can be classified according to its time course, and the duration of its development influences clinical symptoms and presentation. This patient, who was previously healthy, developed acute symptoms of chest pain and dyspnoea due to rapid accumulation of 600mL fluid over 2 weeks. On the contrary, if the fluid is accumulated slowly over months, it allows the pericardium to stretch and adapt, and hence the patient can be asymptomatic. [3]

The morbidity and mortality of pericardial effusion is determined by its aetiology. The aetiology is typically established by the evaluation

Fluid Analysis	<p>Exudative fluid</p> <ul style="list-style-type: none"> • Effusion protein/serum protein - 56/57 = 0.98 (>0.5) • Effusion LDH/ serum LDH - 1835/238 = 7.71 (>0.6) • Effusion LDH - 1835U/L → >2/3 of upper limit of normal serum LDH <p>Cytology: Predominantly neutrophils. No malignant cells. No growth.</p> <p>Immunohistochemistry assessment: Negative</p>
Blood Culture	No bacterial growth.
Autoimmune screen	ANA, ANCA, C3, C4, Rheumatoid factor, ENA antibodies, anti-DNA, CCP – Negative
Viral serology & nasal swab PCR	RSV, rhinovirus, metapneumovirus, adenovirus, parainfluenza, influenza A and B, CMV, enterovirus, coxsackie virus – Negative
Bacterial serology, nasal swab and urine PCR	<i>Bordetella pertussis</i> , <i>Legionella pneumophila</i> , <i>Mycoplasma pneumoniae</i> , <i>Chlamydia trachomatis</i> , <i>Neisseria gonorrhoeae</i> , <i>Treponema pallidum</i> , <i>Streptococcus pneumoniae</i> : all negative
Mycobacterium culture	For tuberculosis – Negative

Table 1. Various investigations performed to evaluate the cause of effusion.

of fluid analysis in relation to the clinical context in which it occurs. Most patients tolerate acute idiopathic effusions well, and have an uncomplicated recovery. In patients with tuberculous pericardial effusions, the mortality is 80 to 90% if left untreated. The mortality is reduced to 8% to 17% with anti-tuberculosis medication. [4] On the other hand, symptomatic effusion is one of the contributing cause of death in 86% of cancer patients with malignant effusions. [5] Conversely, for patients with large, chronic effusions lasting longer than 6 months, up to 50% of them can be asymptomatic. [6]

Cardiac tamponade is one of the most fatal complications of pericardial effusion. Clinically, it can be recognised from Beck's triad of muffled heart sounds, increased jugular venous pressure, and pulsus paradoxus. Our patient had a significant paradoxus of 20mmHg (normal <10mmHg) and elevated jugular venous pressure that made us suspect tamponade on clinical grounds.

In tamponade, increased intrapericardial pressure compromises ventricular filling and reduces cardiac output. This tamponade physiology exaggerates the typical respiratory variation in left and right ventricular filling, which explains the pulsus paradoxus. The time frame over which effusions develop determines the risk of developing a tamponade. An acute accumulation as low as 150ml can result in tamponade. [3]

Echocardiography is essential in the work-up of a patient with pericardial effusion. It demonstrates the size and presence of an effusion, which is visualised as echo-free space (Figure 1). However, the size of the effusion cannot accurately predict the possibility of cardiac tamponade. Cardiac tamponade is a clinical diagnosis. The general rule is pericardial effusions causing tamponade are usually large and can be seen both anteriorly and posteriorly. Other suggestive echocardiographic features of tamponade are right atrial collapse, and right ventricular collapse (Supplementary Figure 2). The sensitivity of identifying right atrial collapse for the diagnosis of tamponade is 50 to 100%, whereas the specificity is 33 to 100%. The sensitivity and specificity in finding right ventricular collapse ranges from 48% to 100% and 72% to 100% respectively. These findings by themselves are unreliable signs of tamponade clinically. They only have diagnostic value if the pre-test likelihood of tamponade is high for the patient in question. [7] It is hard to differentiate haemorrhagic and serous effusion on echocardiograph. However, fibrinous strands on echocardiograph suggest that an inflammatory process is present in the pericardial space, which was seen in this patient's echocardiogram. [8] Hence, the initial suspicion for this healthy young man was cardiac tamponade caused by viral pericarditis.

Significance of haemorrhagic pericardial effusion

Based on the suspicion of viral pericarditis, it was foreseen that the

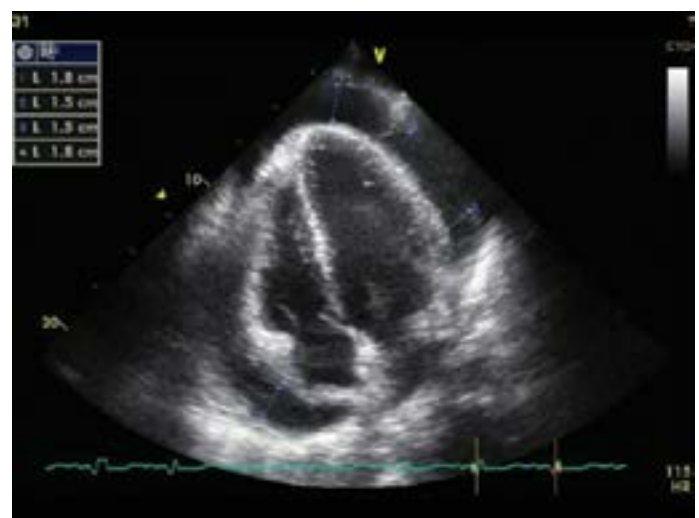


Figure 1. Pericardial effusion in this patient as echo-free space.

Video link: <https://vimeo.com/133111472>

Supplementary Figure 2. Video available online

effusion would be serous. However, it turned out to be haemorrhagic pericardial effusion, which altered the diagnostic and management pathway.

The aetiology of pericardial disease is best categorised based on inflammatory, neoplastic, vascular, congenital and idiopathic causes. It has been noted that a definite cause for pericardial effusion has only been found in 60% of the patients. [1]

There have been major analysis studies addressing the issue of diagnosing and managing large pericardial effusions of unknown origin, [1,9,10] but only one study has discussed the aetiology of large haemorrhagic pericardial effusion. [11] Atar et al's study [11] evaluated 96 cases of haemorrhagic pericardial effusion and highlighted the common causes: iatrogenic (31%), malignancy (26%), postpericardiotomy syndrome (13%), idiopathic (10%). Traditionally, malignancy and tuberculosis have always been considered as potential causes. [2] However, as reflected in Atar et al's study, the incidence of tuberculosis has decreased and there is a rise in cardiovascular procedures over the past decade, resulting in a switch to iatrogenic disease as a major cause. Although it has been known that viral pericarditis can cause haemorrhagic effusions in rare cases, the frequency is unknown.

In our patient, extensive testing was performed to rule out common causes of pericardial effusion. However, no specific cause could be identified and the diagnosis of idiopathic pericardial effusion was made. In patients with idiopathic pericardial effusion, the aetiology is often presumed to be viral or of autoimmune cause. The proliferation of an infective agent and release of toxins can injure the pericardial tissue, causing haemorrhagic inflammation. Additionally, the pericardial involvement in systemic autoimmune conditions is thought to be due to the dysfunction of the innate immune system. [6] His low grade fever, exudative pericardial fluid, neutrophilia, and absent growth in the fluid culture supported the postulation of a viral cause.

Management of idiopathic pericardial effusion

The indications for pericardiocentesis are pericardial tamponade and for effusions more than 20mm, measured in diastole on echocardiograph. [12] When pericardial effusion is associated with pericarditis, management should follow that of pericarditis. The mainstay of therapy for patients with idiopathic pericarditis is nonsteroidal anti-inflammatory agents (NSAIDs), which is aimed at symptom relief. It has been shown that NSAIDs are effective in relieving chest pain in 85 to 90% of patients. [13] While colchicine is the definitive treatment for relapsing pericarditis, a limited number of small trials have also suggested that colchicine alone or in combination with NSAIDs can prevent recurrences when used in the first episode of acute pericarditis. Glucocorticoids should only be used in patients with contraindications or are refractory to NSAIDs and colchicine. [14]

The outcome of patients with large haemorrhagic pericardial effusions is dependent on the underlying disease. The mean survival for patients with malignant pericardial effusion was 8 ± 6 months post pericardiocentesis. In contrast, patients with idiopathic pericardial effusion have a favourable survival outcome similar to the general population. [11] Although no patients had recurrent effusion subsequently in Atar et al's study, it is known that with acute idiopathic pericarditis, there is a 10-30% chance of developing recurrent disease, and often with an effusion. A single recurrent attack may happen within the first few weeks after the initial attack, or as repeated episodes for months. [15,16] The pathogenesis of recurrent pericarditis is unclear,

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but has been speculated to be due to an underlying autoimmune process. [16] With recurrent episodes, the repeated inflammation can lead to chronic fibrotic scarring and thickening of the pericardium, resulting in constrictive pericarditis. [6]

There is no specific feature that reliably predicts the recurrence of idiopathic effusions. However, it has been shown that patients who responded well to NSAIDs have a lesser chance of recurrence, [17] while initial treatment with corticosteroids favours occurrence of recurrences due to deleterious effect on viral replication. [18] This patient had a good response to NSAID within a week with improvement in his symptoms, which subsequently fully resolved. This further supports the diagnosis of idiopathic pericarditis and is also a good indicator that he is not at an increased risk of recurrence. However, it would be beneficial for this patient to be reviewed in the future with repeat echocardiography if clinically warranted.

Conclusion

Cardiac tamponade is a life-threatening medical emergency that requires prompt diagnosis and emergent treatment. It is essential for one to be able to recognize Beck's triad. Haemorrhagic pericardial effusion is a red flag that warrants a meticulous search for uncommon but sinister aetiologies, especially malignancy and tuberculosis, as the mortality rate is high if left untreated. When extensive investigations have been conducted and the diagnosis of idiopathic pericarditis is made, NSAIDs are the mainstay of therapy. Colchicine can be considered to prevent recurrence, while glucocorticoids should only be used as a last resort.

Consent declaration

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

Conflict of interest

None declared.

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The management of adnexal masses in pregnant women: A case report and review of literature

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Chris is an enthusiastic teacher of Obstetrics and Gynaecology and encourages medical students (and junior doctors) to question their practice, challenge the dogmas of their speciality, and continually develop their clinical and surgical skills to best serve their patients.

A 33 yr old woman presents with irregular menstrual bleeding and on examination has bilateral adnexal masses. At this original presentation, she was unexpectedly pregnant in the first trimester. Throughout her pregnancy these adnexal masses were presumed to be benign ovarian dermoids. However, at caesarean section the appearances were suspicious. Histological studies confirmed the presence of bilateral ovarian mature teratomas but also of a mucinous intestinal borderline tumour. A literature review of the management of adnexal masses in pregnancy is included.

Introduction

The diagnosis of adnexal masses during pregnancy has become increasingly common due to the widespread use of routine antenatal ultrasounds. [1-4,22] Despite the advancements in ultrasound technology, incidental adnexal masses are still being identified during caesarean section. [1,5,6] Although the management of adnexal masses may differ if diagnosed during pregnancy or at caesarean section, the diagnostic limitations of antenatal ultrasonography may result in modifications in intraoperative or postpartum management.

Case Study

A 33 year old nulliparous woman presented to her general practitioner with concerns about irregular menstrual cycles that she had been experiencing since menarche at 13 years of age. The cycle duration was reported to be 30-90 days in length with a bleeding duration of approximately 7 days. The bleeding was described as "not heavy". She was in a long-term relationship and not using any form of contraception. She denied any pelvic or abdominal pain and had no gastrointestinal or genitourinary symptoms. She also denied any abnormal vaginal discharges or previous history of sexually transmitted diseases. Her cervical smears were up to date and had been consistently reported as "normal". She had no past medical or surgical history but a strong family history of type 2 diabetes mellitus.

On examination, she appeared well and comfortable. Her abdomen was soft and non-tender. Speculum examination did not show any cervical abnormalities, however, on bimanual examination bilateral non-tender adnexal masses were found. A positive urine pregnancy test was also detected.

A pelvic ultrasound demonstrated a bicornuate arcuate uterus and bilateral adnexal masses. The right adnexal mass measured 41x32x32mm and the left measured 72x59x64mm. Both masses were described as being echogenic, with no shadowing and no evidence of increased vascularity. The report suggested that the features exhibited were of bilateral ovarian mature teratomas (ovarian dermoids). Due to this, tumour markers, such as CA-125, were not performed. She was approximately 12 weeks pregnant at the time of the scan.

Throughout the pregnancy, pelvic ultrasounds were performed. These demonstrated an increase in the size of both adnexal masses. By 31 weeks of pregnancy the right ovary measured 140x110x65mm and the left ovary measured 77x52x55mm. No further ovarian changes were



identified in subsequent ultrasounds up to the delivery date.

During the pregnancy the patient developed gestational diabetes mellitus that was poorly controlled resulting in a lower segment caesarean section being performed at 36 weeks of gestation. The preoperative plan was to perform a bilateral cystectomy at the time of the procedure. This was based on the patient's age, parity and the assumed benign nature of the ovarian masses.

Intraoperatively, a bicornuate arcuate uterus was identified with bilaterally enlarged ovaries (Figure 1). A bilateral cystectomy was performed without spillage of their contents, sparing the remaining ovarian tissue. Peritoneal washings were also taken for cytology based on the intraoperative findings of an unusual surface appearance of the right ovary (Figure 1). Following the operation, both cysts were bisected (Figure 2). The left cyst had typical dermoid features of sebaceous material and hair (Figure 3a). However, the right cyst had additional unusual features predominately of multiple mucinous cysts (Figure 3b). Both cysts were sent for histopathology. The post-operative period was uneventful and she was discharged on day four.

The histopathology report confirmed the left cyst to be a benign mature teratoma. However, the right cyst was reported as a mature teratoma together with a mucinous intestinal borderline tumour component. The peritoneal cytology did not reveal any evidence of malignant cells.

Discussion

Adnexal masses are detected in approximately 1-4% of all pregnancies. [2,9,10,24] In most cases, the adnexal mass is diagnosed incidentally on routine antenatal ultrasounds in an otherwise asymptomatic patient. [2,8-10] However, in some cases the patient can present with symptoms such as pain and/or signs of a palpable mass. [2] In this case study, the patient did not present with any abdominal pain; however on examination bilateral adnexal masses were palpable which were also confirmed on ultrasound scan.

The majority of adnexal masses are of ovarian origin, [2,9] however others may arise from extra-ovarian structures such as the fallopian

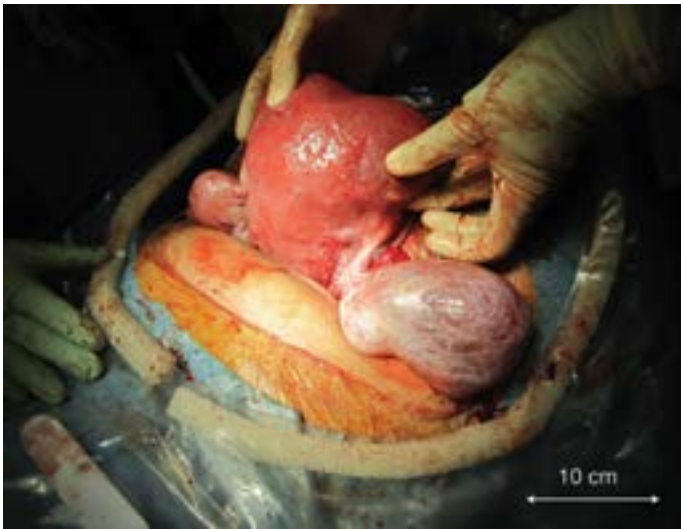


Figure 1. Macroscopic appearance of the bicornuate arcuate uterus and bilaterally enlarged ovaries.

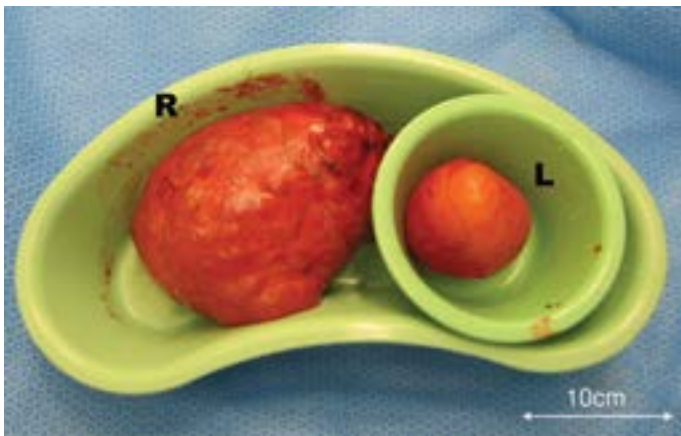


Figure 2. Macroscopic appearance of the left (L) and right (R) cysts following cystectomy.

tubes, uterus and non-gynaecological tissues (Table 1). Frequently encountered ovarian masses in pregnant women include: mature cystic teratomas, cystadenomas and functional cysts. [5,6] In most cases, the adnexal pathologies are unilateral. [3,5,7] In cases with bilateral masses, the most frequent diagnosis is ovarian cystic teratomas. [5] In this case study, the preoperative ultrasound reports suggested that the bilateral masses were also ovarian teratomas.

Ultrasonography is the imaging modality of choice for detecting adnexal masses in both pregnant and non-pregnant women. [4,11] However, ultrasonography has limitations and not all adnexal masses during pregnancy are detectable as the gravid uterus may obscure the visualisation and detection of such masses. [1,5] Although ultrasonography may assist in differentiating benign from malignant adnexal masses, [4,10,18,23] it is not useful in differentiating between benign and low malignant potential tumours preoperatively. [17] This was highlighted in this case report, whereby the right cyst was reported as showing features suggestive of a benign mature teratoma and therefore, a cystectomy was performed. Subsequent histological analysis provided a diagnosis of a borderline tumour, where a salpingo-oophorectomy may have been the procedure of choice.

The management of adnexal masses detected during pregnancy is controversial. Both expectant and surgical approaches, each carrying specific risks and benefits, are possible. Factors including size, gestational age and sonographic appearance may influence the final management. [7,9]

Most adnexal masses detected during pregnancy will resolve spontaneously or significantly reduce in size without any interventions.



Figure 3a. Bisected left cyst showing typical dermoid features.

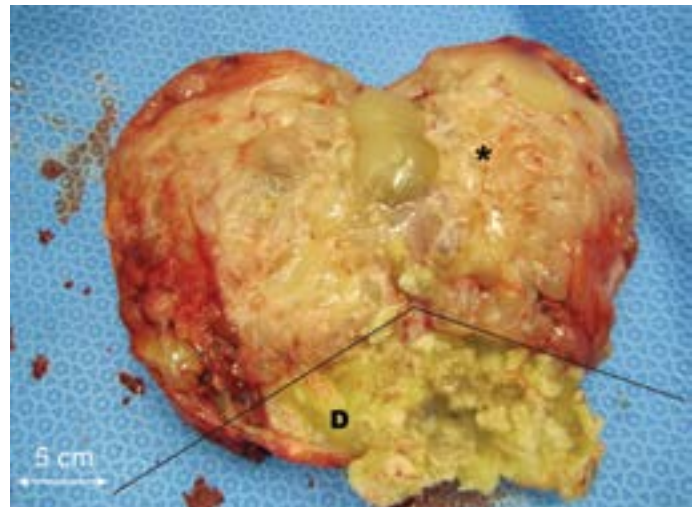


Figure 3b. Bisected right cyst showing features of a dermoid cyst (D) and multi-loculated cysts (*). The line demarcates the dermoid-type tissue inferiorly and the mucinous component superiorly.

[2,8-11,15] Furthermore, only 2-8% of adnexal masses are malignant. [7,22] Therefore most masses during pregnancy can be managed expectantly, [8,9,15] particularly if they are asymptomatic, less than 5-6cm in diameter, have a simple sonographic appearance and are diagnosed before 16 weeks of gestation. [8] However, serial observations and ultrasound scans throughout the pregnancy are recommended to monitor potential changes in these masses. [15] The masses may then be managed surgically at caesarean section or have repeat imaging performed 6-8 weeks post-partum in the case of vaginal deliveries. [15] However, some of the risks associated with this conservative approach include: torsion, cyst rupture, infection, obstructed labour or a delayed diagnosis of malignancy. [1,3,8,12,25-29]

By contrast, a surgical approach is indicated for those patients with adnexal masses during pregnancy that are symptomatic, greater than 5-6cm in diameter, have a complex sonographic appearance suggesting malignancy, or persist into the second trimester. [2,8] The ideal window for surgical intervention in pregnant women is in the early-mid second trimester, to reduce the risk of complications. [10,13] These complications include: spontaneous miscarriage, spontaneous rupture of the membranes, preterm labour, preterm birth and intrauterine growth restriction. [2,10,13,14] However, it is unknown whether these complications are due to the effect of surgery or anaesthesia. Although laparoscopy or laparotomy may be performed, particularly in the second trimester, laparoscopic surgery is considered more beneficial to the mother with few studies suggesting an effect on the developing fetus. [20,21]

The impact of adnexal masses on the developing fetus is largely

Ovarian	Extra-Ovarian
Benign: <ul style="list-style-type: none"> • Simple cyst • Haemorrhagic cyst • Serous cystadenoma • Mucinous cystadenoma • Endometrioma • Luteoma • Brenner tumour • Ectopic ovaries Malignant: <ul style="list-style-type: none"> • Epithelial tumours • Germ cell tumours • Sex cord stromal tumours • Borderline tumours • Metastatic tumours 	Tubal: <ul style="list-style-type: none"> • Paratubal cyst • Tubo-ovarian abscess • Hydrosalpinx • Fallopian tube tumour Uterine: <ul style="list-style-type: none"> • Uterine leiomyomas Non-Gynaecological <ul style="list-style-type: none"> • Appendiceal abscess • Diverticular abscess • Mesenteric cyst • Pelvic kidney • Lymphoma

Table 1: The aetiology of adnexal masses detected during an intra-uterine pregnancy [2,9,10]

affected by the natural history of the adnexal mass. Most adnexal masses within Table 1, in-and-of-themselves will not directly affect fetal development. However, iatrogenic surgical procedures, whether as prophylactic or reactive interventions, may result in miscarriage or premature labour. Rarely, is premature delivery indicated to deal with the adnexal mass. However, in the term pregnancy, a caesarean section may be possible at the same time.

Generally, corticosteroids and tocolytics are not administered prophylactically for surgical procedures dealing with adnexal masses in pregnancies greater than 24 weeks of gestation. They may, however, be indicated following surgery. [30]

For those adnexal masses that are detected incidentally during caesarean section, it is recommended that they be removed. [1,4] The recommended procedure is a cystectomy, whilst oophorectomy and salpingo-oophorectomy procedures may also be considered. [16] The rationale is to exclude the possibility of malignancy and to avoid the need for further surgical procedures following the caesarean section. [1,5,16]

In this case report, the adnexal masses were managed with an expectant approach, despite their increasing sizes and persistent nature throughout the pregnancy. A bilateral cystectomy was performed at caesarean section on the assumption that the masses were teratomas, which are predominately benign tumours. [19] However, the histological diagnosis differed and revealed a tumour with borderline malignant potential. A different management approach may have been taken if this was suspected during the pregnancy.

This case report demonstrates the diagnostic limitations of ultrasonography and the potential dependence on this modality in the

management of adnexal masses in pregnancy.

Summary Points

1. The diagnosis of adnexal masses during pregnancy has increased due to the widespread use of ultrasonography.
2. Although ultrasonography is useful in diagnosing adnexal masses, there are limitations.
3. The management of adnexal masses during pregnancy is controversial. There are two approaches, including an expectant and a surgical approach.
4. The recommended management approach for incidental masses detected at caesarean section is extirpation.

Consent Declaration

Consent to publish this case report (including photographs) was obtained from the patient.

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Conflict of Interest

None declared.

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Clavicle fractures: An audit of current management practices at a tertiary hospital, a review of the literature and advice for junior staff

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The complete version of this audit was awarded the Richard Taunton Southwood Prize for Orthopaedic Research for best Orthopaedic audit 2014. Dr. George has presented on the topic of clavicle fractures at both state and national Orthopaedic conferences throughout 2014/15.

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Professor Jaarsma is the head of Orthopaedic Trauma at Flinders Medical Centre and a Professor of Orthopaedics at Flinders University overseeing all student audits in the department of Orthopaedics.

Background: The clavicle is one of the most commonly fractured bones in the body. Interns are often delegated to treat these cases in an emergency department. This audit looks at the adherence to a tertiary hospital's clavicle fracture protocol and reviews the literature to provide suggestions on updates based on current evidence. **Methods:** A retrospective case note and radiograph audit was undertaken to assess adherence to current protocols for the calendar years 2012 and 2013. A literature search was performed to find the most up to date evidence for future clavicle fracture management. **Results:** There were 131 clavicle fractures reviewed. An AP x-ray was taken in 120/122 cases (98.3%). The Orthopaedic registrar was notified for 6/7 (86%) cases with respiratory, neurovascular or skin compromise. Up to 83/131 (63%) patients were provided with a broad arm sling. Mean initial follow up was at ten days (3-20 days) and 39/95 (41%) followed x-ray protocol at this review. Appropriate rehabilitation advice was documented in 12/82 (14.6%) cases and the mean duration until discharge was 52.25 days. **Conclusion:** Despite the high frequency of clavicle fractures there are still significant errors that can be, and are being, made in their management. It is important for all medical students and junior doctors to become familiar with this Orthopaedic condition, as it is a common presentation that is often initially managed by junior medical staff.



management, and rehabilitation of clavicle fractures. Additionally, the hospital intranet was searched for any further documents including protocols, information sheets, and patient handouts. Consultation with the physiotherapy (PT) and occupational therapy (OT) departments was undertaken to assess any current gold standards, best practice or unwritten guidelines.

The case notes and radiographs of patients identified with a clavicle fracture were reviewed and adherence to the current protocol was assessed. Specifically, adherence to the following aspects of the protocol was scrutinised (Figure 1).

1. All patients are to receive an anterior to posterior (AP) x-ray
2. The orthopaedic registrar must be notified if there is respiratory, neurovascular or overlying skin compromise
3. All patients are to receive a broad arm sling for acute management
4. Outpatient follow up is to be booked for two weeks post injury
5. Only postoperative patients are to have an x-ray on arrival (XROA) at the two week follow up
6. All patients are to begin pendulum exercises immediately, range of motion (ROM) from two weeks, full active ROM (AROM) from 6 weeks or after clinically healed
7. Return to sport (RTS) should be delayed for at least 4-6 months.

Ethical approval

This audit was reviewed and approved by the local clinical human research ethics committee. No identifiable patient data was collected and all records were viewed on site in the medical records department. A retrospective case note and electronic record audit was performed for the calendar year of 2013. As insufficient data was available to make reliable conclusions an additional calendar year, 2012, was included.

Patient recruitment

With the assistance of the orthopaedic department and the support of the project manager, all patients with clavicle fractures who presented to the emergency department (ED) or who were admitted to the wards in the calendar years 2012-13 were included. The hospital coding system, Inpatient Separations Information System (ISIS), was searched using the World Health Organisation (WHO) International Classification of Diseases, version ten, (ICD10) codes for all clavicle fracture admissions, S4200-3 inclusive. In addition the ED database for

Introduction

Clavicle fractures are one of the most common fractures in the adult with an annual incidence of 29-64 per 100,000 people, per year. [1] Fractured clavicles account for up to 5% of all fractures and up to 44% of fractures to the shoulder girdle. [1,2]

Clavicle fractures are commonly managed by junior staff, and the current adult fracture protocol at our institution guides this management (Figure 1). The protocol was issued in July 2006 and reviewed in 2009. However, this protocol remains based on evidence the most recent of which was published in 1997. [3-8] There has been an influx of published literature on clavicle fractures over the last decade providing more recommendations for which an updated protocol can be based, including two well-designed multi-centre randomised controlled trials. [1,9,10,11,12,13] These articles demonstrate the shift from conservative management to surgical management for displaced and comminuted fractures of the adult clavicle.

This retrospective case note and radiograph audit firstly assesses the adherence of management practices at a tertiary hospital to the current institutional protocol for the calendar year of 2012 and 2013. Secondly, it discusses the standards of best practice in the current literature, with the view to providing recommendations for alterations to hospital protocol and management practice.

Methods

Process

In preparing for this audit a literature review was conducted to identify the gold standard and best practice guidelines for the investigation,

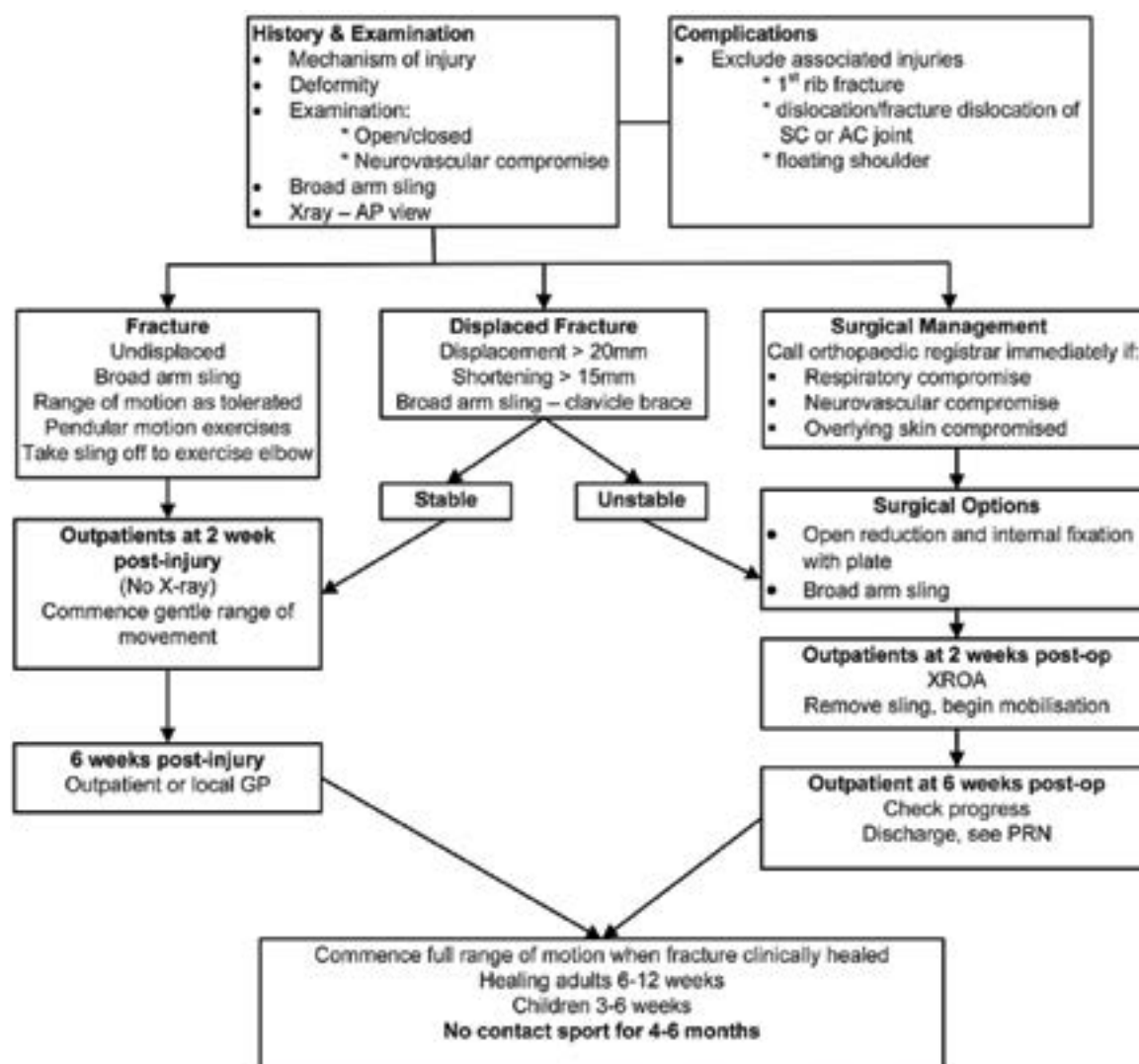


Figure 1. The current adult clavicle fracture protocol for which adherence was audited.

the two calendar years was hand-searched for provisional diagnoses relevant to clavicle fractures. This limited selection bias caused by spelling errors if searched electronically. These searches provided a list of 141 patient unit record numbers (URN) that were provided to medical records for retrieval.

Data retrieval

All case notes were reviewed immediately once available to minimise loss to the removal of records. Missing records were re-requested and viewed on multiple occasions until all records had been accounted for. Despite multiple searches two case notes were unable to be retrieved, being listed on the system as in stock but unable to be located by staff. For these two cases the electronic records were viewed to minimise selection bias and to ensure all patients were analysed.

Each patient file was meticulously studied and cross-referenced against the electronic discharge summaries and encounters, in addition to radiological analysis using a picture archiving and communication system.

Data analysis

Data was collected and stored in a Microsoft Excel (Copyright Microsoft Corporation 2010) spreadsheet. Simple descriptive statistical analysis was performed using IBM SPSS version 22 (Copyright IBM Corporation and other(s) 1989, 2013).

Standards for adherence

In consultation with the orthopaedic department it was determined that 90% compliance with the current protocol would be deemed acceptable. Adherence was analysed collectively for the entire

cohort but also separately for the two calendar years, surgical versus non-surgical patients, and then again against current literature recommendations. Only the collective data will be presented.

Results

Recruitment and demographics

The database searches resulted in the retrieval of 141 patient URNs. Of these 131 were new clavicle fractures. There were 99 males and 42 females of which 47 fractures were on the right and 84 on the left (Table 1). The dominant arm was affected in 17 cases, non-dominant in 34, and not documented in 80 cases. There were three medial (2.3%), 93 central (70.1%) (Figure 2), 34 lateral (25.9%), and one both middle and lateral (other 0.8%). This is almost identical to the fracture pattern distribution reported by Robinson. [11] Associated injuries were documented in 34/131 (26%) cases. This is slightly less than the 36% reported by Nowak, Mallmin & Larsson however there are differences between the skin abrasions that were included in each study. [14]

Radiological adherence

An AP radiograph was taken for 120/122 (98.3%) patients (nine outside films). The two patients that did not have an x-ray both re-presented and subsequently had an x-ray identifying a clavicle fracture and were therefore included in this audit. Only 97/122 (79.5%) had two views taken of their clavicle fracture on presentation despite current literature and orthopaedic dogma dictating that every fracture should be viewed from two angles and include two joints. [15,16]

At the two week review 39/95 (41%) cases followed protocol regarding XROA. The conservative group were not required to have an x-ray at

MOI		N	Minimum age	Maximum age	Mean	Std. Deviation
Sport (22.7%)	Male	28	10	47	21.82	8.994
	Female	2	12	35	23.50	
	Total				21.93	
Bicycle (24.2%)	Male	29	11	57	35.14	13.671
	Female	3	54	59	56.33	
	Total				37.12	
MBA (11.4%)	Male	15	18	55	30.40	10.622
MVA (3.8%)	Male	1	34	34	34.00	26.073
	Female	4	26	82	55.75	
	Total				51.40	
Fall low energy (15.9%)	Male	9	40	92	63.44	25.037
	Female	12	1	98	66.83	
	Total				65.38	
Fall high energy (18.9%)	Male	15	1	60	17.53	14.271
	Female	10	3	36	13.50	
	Total				15.92	
Direct Blow (2.3%)	Male	2	3	15	9.00	8.737
	Female	1	20	20	20.00	
	Total				12.67	
Not specified (1%)	Male	1	15	15	15.00	-
	Total	/131				

Table 1. Distribution of injury across the cohort. MOI = Mechanism of Injury, MBA = Motor bike accident, MVA = Motor vehicle accident, N = Number of patients, Std. = Standard.



Figure 2. The typical middle third clavicle fracture that presents a management dilemma.

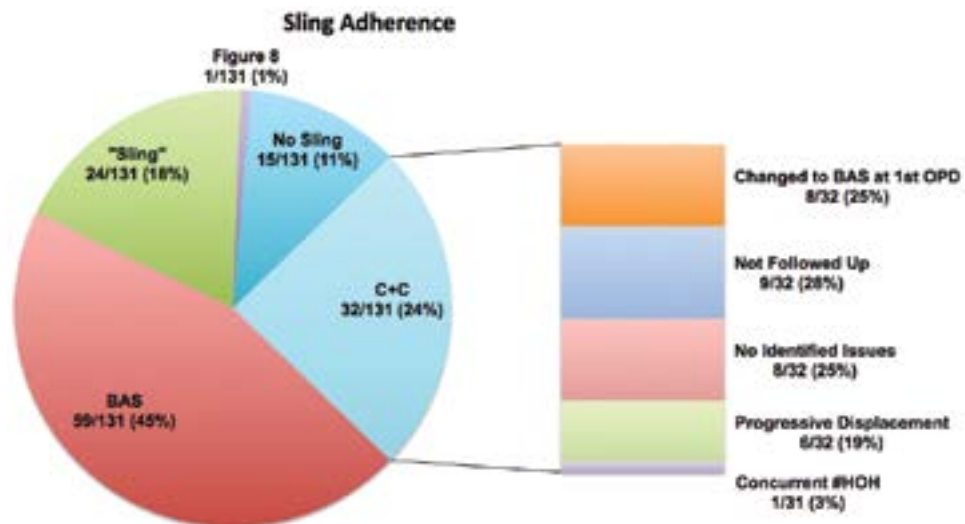


Figure 3. Illustrating the adherence of staff to provide a broad arm sling as first line management. BAS = Broad Arm Sling, C+C = Collar and Cuff, #HOH = Fractured Head of Humerus, OPD = Outpatient Department.

	N	Minimum	Maximum	Mean	Std. Deviation
Surgical Age	14	18	56	37.57	13.043
Private Referral Age	11	18	48	29.67	9.862

Table 2. Summary of the age distribution of patients treated surgically or those who elected for a private surgeons care. N = Number of patients, Std. = Standard

two weeks with adherence in 30/85 (35.3%), however, 13 of these had x-rays at subsequent appointments. For the conservative cases that did have x-rays at their first outpatient department (OPD) appointment 3/55 (5.5%) resulted in a change of management toward surgery. Nine out of ten (90%) surgical patients had an x-ray to check the position of the metalwork at two weeks as required.

Broad arm sling

Compliance with the protocol regarding the broad arm sling application is summarised in Figure 3. Of note 6/32 (18.8%) patients who were provided with a collar and cuff for acute management showed progressive displacement and five of these required surgical fixation. If the benefit of the doubt is given and all those who were documented as given a 'sling' are combined with the BAS then 83/131 (63.3%) patients were correctly treated.

Registrar notification

The orthopaedic registrar was notified 46 times for the 131 cases analysed (35%), although according to the protocol they are only required to be notified if there is respiratory, neurovascular, or skin compromise. In this case they were notified on six out of seven occasions (86%). However, if they were also required to be notified for displaced fractures >20mm and shortened >15mm in addition to the associated injuries in the protocol, then they were notified in 27/51 (53%) cases. Cases of which the orthopaedic registrar was not informed of include one floating shoulder, three ACJ separations, one head of humerus (HOH) fracture, and one patient with ipsilateral rib fractures 1-5.

Prior to the outpatient follow up six patients re-presented to ED, two patients on multiple occasions. Of these two were treated with a collar and cuff and one with a sling.

Complications or associated injuries were present in 18/131 cases (13.7%), five with tented/compromised skin, six ACJ separations, four floating shoulders, one ipsilateral HOH fracture, one ulnar nerve paraesthesia, and one patient with multiple ipsilateral rib fractures. Of these six underwent surgical fixation.

There were 14 surgeries (11 middle third, three lateral) and eleven patients received private orthopaedic management (Table 2).

Rehabilitation

There were 82 patients followed up in the orthopaedic OPD clinic. Twelve of these (14.6%) had sufficient documentation to suggest the patient had been provided with appropriate rehabilitation advice. These included 4/9 (44%) surgical cases and 8/73 (11%) conservative cases. This left a large cohort of patients that had been given some or no advice on what rehabilitation they could perform. Six patients attended their six-week review having been immobilised in their sling for the entire duration leading to stiff painful shoulders. In eight case notes there is mention of seeking physiotherapy treatment of which two cases were treated by the hospitals physiotherapy department. There are no current physiotherapy handouts or protocols and the occupational therapy department has no involvement in the management or rehabilitation of clavicle fractures.

Discussion

Clavicle fractures are a common presentation to any emergency department, representing 5% of all fractures, and are often managed by junior staff. This audit demonstrates that there is still some mismanagement and that further education of junior staff is required.

Rehab stage	N	Timeframe
Pendulum	16	Immediately to 4/52
ROM	16 (22.9%)	9 days to 6/52
AROM	16	4 – 8 weeks
RTS	15 (21.4%) /70	6 weeks to 4 months

Table 3. Rehabilitation timeframes. This table presents information on the advice given and the timeframes for patients other than the 12 patients deemed to have been given correct advice. It is not the same patients in each group. N = number of patients, ROM = Range of Motion, AROM = Active range of motion, RTS = Return to sport

The gold standard for initial radiological review of clavicle fractures remains to be elucidated but current evidence agrees on the standard AP radiograph plus a second radiograph tilted on an angle. [15,16,17] Only 97/131 (74%) patients received two different views of their clavicle fracture on presentation. The angle of the second view ranged from 5-30 degrees AP cephalic tilt, with each five-degree increment in between. The optimal angle and direction of this second radiograph varies among authors with some recommending a posterior to anterior (PA) 15-degree cephalic tilt, while others recommend an AP 15-degree caudal tilt. [15,16,17] This makes it difficult to compare fracture patterns between clavicles when determining clinical management and also for future retrospective analysis. It may be preferable to have two views from the same side to limit the manoeuvring of patients and reduce the time demand on the radiological department. A second AP view with 20 degrees cephalic tilt has been recommended and would be the technically easiest view with minimal changes to current practices. [9]

Conservative treatment remains the management of choice for isolated non-displaced clavicle fractures. [12,18] The broad arm sling is recommended for clavicle fractures, [19] as the collar and cuff allows traction on the arm that risks further displacement of fracture segments. [20,21] The figure-of-eight slings have not been shown to be superior to the broad arm sling and are more uncomfortable and difficult to use. [22] Our results demonstrate that the collar and cuff is still being provided in many cases over the preferred broad arm sling. This may be due to confusion with the fractured neck of humerus that requires distracting forces for fracture alignment. One fifth of patients provided with collar and cuffs demonstrated significant progression of fracture displacement with many of these requiring surgical fixations.

While most isolated non-displaced fractures of the clavicle are managed conservatively, it is important to know when to refer to the orthopaedic department for review. Clear operative indications include compromise to the skin, nerves, vasculature, and grossly displaced/comminuted fractures. [23] Some authors also advocate for the primary fixation of clavicle fractures with multi-trauma, ipsilateral shoulder injuries, acromioclavicular joint (ACJ) involvement, high velocity mechanisms, or young active individuals. [24,25] For these patients, the surgeon's preference continues to dictate treatment. [26] As such it is difficult to create a protocol to mandate management and the protocol is rather a guide to prompt management considerations.

Furthermore, over the past ten years there has been a growing body of literature increasing the relative and absolute surgical indications for clavicle fractures [13,23,24,27] Newer studies have highlighted

that previously used outcomes may not be the best end points for assessing management. Previously, radiological union was the sole primary outcome for assessment of fracture management. [18,28] Recent studies focussing on patient-centred outcomes such as pain and functional capacity however have highlighted a disparity between radiological union and satisfactory objective and subjective patient-centred outcomes. [9-14] Furthermore, older studies have included children in outcome assessments, despite the greater regenerative capacity of this younger age group prior to fusion of the medial growth plate, leading to an over estimation of adult clavicle fracture recovery in these older studies. [20]

Recent studies have demonstrated sequelae including pain and neurological deficits occurring in up to 46% of clavicle fractures. [29] These sequelae are more likely in non- or mal-union of the fracture. Non-union rates for adult patients are as high as 15% and symptomatic mal-union up to 20-25%. [13] Risk factors for non-union include:

- Smoking (33.3%)
- Increasing Age and Female gender (often less symptomatic in this population)
- Shortening >20 mm (increasing shortening increases non-union/mal-union)
- Displacement >15 mm (27%)
- Comminuted fractures (21.3%). [24,30]

The non-union rate for surgically treated patients' is around 1-2%. [9,10,13] The number needed to treat (NNT) if all displaced clavicle fractures were operated on to prevent one symptomatic non-union would be 7.5, this number is reduced to 4.6 if symptomatic mal-unions are included. [13,24] The NNT drops to 1.7 if only those with multiple risk factors for non-union were surgically fixed. [24] Surgical risks must be considered however, including infection, implant irritation, neurological damage, and even death. [9,10,31] For widely displaced mid third clavicle fracture surgical plate fixation has been shown to be superior to conservative management. [9,10]

In this audit, the orthopaedic registrar was notified for most cases where there was neurovascular, respiratory, or skin compromise. However, in the current protocol there is mention of displacement and shortening with a decision to be made on whether the fracture is stable or unstable and whether the patient receives surgical or conservative management. If the orthopaedic registrar was required to be notified to make this decision then they were only notified in half the cases. It may be seen as an increased demand on the ED if they had patients waiting in beds for an orthopaedic review if it was considered unnecessary.

Murray and colleagues have shown that shortening and displacement are risk factors for non-union and it has been shown that delaying surgery results in worse functional outcomes. [24,32,33] Hence, it would be prudent to have an orthopaedic review in ED to make the clinical decision regarding management immediately. While this would increase the demand on orthopaedic staff to review x-rays and or patients from ED it also has the potential to decrease outpatient demand. By providing patients with the correct treatment immediately, early (< 2 weeks) outpatient follow up can be avoided and the six representations to ED potentially avoided. Additionally if more accurate predictions are made for probable outcomes then work loads can be reduced by minimising the patients that are treated for extended periods or who fail conservative treatment and undergo additional surgical fixation.

There was a large variation in time to outpatient follow-up after ED discharge. This potentially reflects the uncertainty of the ED staff in their management of the patient. Rather than discharging the patient with appropriate sling, pain medication, and early rehabilitation advice they are requesting very early orthopaedic outpatient follow up essentially doubling the patient's visits.

Radiological evaluation at the two-week review was over-utilised

with correct use in less than half of the patients. This again could reflect uncertainty among medical staff about management. Of the 55 conservative patients undergoing multiple x-ray evaluations, a change in management was only initiated in three cases. Progressive displacement of the fracture ends has been recognised in one third of cases over a 5-year period by Plocher et al. who recommends serial x-rays for the first 3 weeks. [25] However, repeated x-rays are not useful unless the information is going to be used to guide clinical decision-making. Again, identifying patients at risk of progressive displacement (such as high velocity injuries) or those on the cusp of surgical intervention and providing early decision-making could remove the need to wait and watch.

Advice on rehabilitation was poorly documented and may reflect that it was not provided adequately in many cases. Documentation of education provided is an important part of keeping legal records and only one-fifth of patients had documented evidence that rehabilitation advice was provided. It was evident that no advice had been given for the six patients that returned to the six-week review having remained immobilised in the sling. Rehabilitation timeframes are largely based on expert opinion and are generally consistent with the current practices. [9,20,34] There has been limited research into the optimal timeframe to return to sport, however one study followed 30 patients after plate fixation and 20 had returned to sport after twelve weeks. [35] Three conservative patients re-fractured within 3-5 months in our audit population suggesting that returning to full contact sport should be delayed greater than six months.

The reliability of the results provided is limited by the dependence on multiple steps in accurately identifying and documenting clavicle fractures. These factors include:

- Staff in ED diagnosing the clavicle fractures and documenting accordingly
- Administration clerk in ED transcribing appropriate provisional diagnoses
- Hospital coding officers applying the correct ICD10 codes
- Human error is possible in misidentifying data in the notes
- Human error in transcribing data into SPSS
- Especially dependent on the accuracy of the doctor's written case notes and discharge summaries for the above steps and also audit data collection.

Every effort was taken to ensure that the data collected was accurate including cross-referencing across multiple platforms. In stating this, however, the data collection for the variables dependent on documentation can only be as accurate as the written information and may not be a true representation of actual events. This would impact most significantly on the reporting of the sling provided, orthopaedic registrar notification, and rehabilitation advice given.

The methods used do not capture the cases that were directly referred to the outpatient department without first presenting to ED or as an inpatient. However, the majority of this audit involved looking at the initial management, as per the protocol, and therefore these cases were not required.

Conclusion

Clavicle fractures are a common presentation to any emergency department and are often managed by junior staff. This audit demonstrates that there is still some mismanagement, particularly in radiological assessment, sling prescription, and knowledge of protocol for registrar notification, outpatient follow-up and rehabilitation. Furthermore, new evidence indicates that the current protocol at this institution requires updating to clarify the requirements for referral and allow earlier interventions or rehabilitation. In summary, recommended radiological views are a standard AP and a second AP with 20 degrees cephalic tilt. Isolated non-displaced fractures of the clavicle are almost always managed conservatively, however, it is important to know when to refer to the orthopaedic department

for review. This is always necessary if there are associated injuries or pending complications. It is also recommended that all displaced or comminuted fractures be referred for an orthopaedic opinion. The broad arm sling is the immobilisation technique of choice and not the collar and cuff for clavicle fractures because the collar and cuff allows distracting forces that risks further displacement of the fracture segments. Early rehabilitation is required to prevent painful stiff shoulders.

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Conflict of Interest

None declared.

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Medicine in Kathmandu

Emma Cole

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In the summer of 2014/15 I travelled to Kathmandu in Nepal to undertake a four-week medical elective in the Kathmandu Teaching Hospital. I also spent an additional one-week living with a family in a rural village as part of Work the World's Village Healthcare Experience add-on.

I was lucky enough to spend those four weeks working in the surgical department, alternating between the general surgical GI team and the neurosurgical team. Whilst I found it difficult to be as hands-on in these teams as I would have hoped, I observed surgeries and diseases that I wouldn't have had the opportunity to see in Australia. Most surgeries were critical, complicated and painstakingly long. And the list of diseases I witnessed was rare, complex and advanced.

Being proactive is the key to a successful elective. The more questions you ask and interest you show, the more opportunities you'll be given to learn. Because the hospital is a teaching hospital, students don't look out of place here either. I felt completely integrated into my teams and had the opportunities to ask questions and for my supervisors to provide the explanations - when possible! Many of the doctors spoke English fairly well too, which was a relief especially when almost all of your patients do not.

The highlight of this trip was undeniably living among the Nepalese in a small village in the mountains. The experience to live as they do was unforgettable. Every day was a new adventure and the community was so welcoming. But working at the local health clinic was a real learning experience. The lack of understanding but pure appreciation from the patients, even though we did very little for them, still astounds me. I even got to be the doctor for the week!

I can't imagine having this experience anywhere else but Kathmandu. The destination itself offered so much. On the weekends we were able to take trips to the surrounding countryside, hike at Shivapuri Nagarjun National Park and take a short flight to Pokhara where I was lucky enough to see the Annapurna mountain range from the Buddha Stupa. At the end of my elective, I also spent a week trekking to Annapurna base camp. Incredible!

My elective was the most amazing experience I have had yet and I would definitely recommend it, and Work the World, to anyone who was interested in gaining some experience in a third world country.



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Epidural analgesia during labour: Friend or foe? A reflection on Medicine, Midwives and Miranda Kerr

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Choosing a method of pain relief for childbirth is an extremely personal, and often well-considered, decision. For many women, childbirth is the most painful experience they will ever encounter. It is no surprise that a number of pharmacological and non-pharmacological methods have been developed to help manage this painful and sometimes traumatic experience. In Western cultures, epidural analgesia (EA), as well as a number of other methods, is widely used, and its benefits (and risks) are well documented. [1-3] Despite the generally positive evidence base, many women choose not to use EA during their labour. [1,4,5] Clearly, there are other factors that influence their choice of pain relief (or lack thereof). Personal attitudes towards the acceptability of labour pain and fear of the process are key, but outside influences can be significant. [1,5,6] Those around her – her doctors and/or midwives, her family and friends – will almost certainly have shaped her attitude. However, public pressure generated by celebrities such as Miranda Kerr may influence a woman's decision more than we realise. In the age of social media, where opinions are abundant and conflicting, women may be more confused than ever: is an epidural a friend or a foe?

There are a number of methods available for managing pain during the labour process. In discussing these options it often becomes a balancing act between what the woman considers to be an acceptable level of pain, with an acceptable level of risk – a highly personal decision that relies on a woman being able to adequately understand the risks and consequences. Options for analgesia may be non-pharmacological, such as massage, breathing exercises and transcutaneous electrical nerve stimulation (TENS), which have limited evidence of efficacy but appear to improve satisfaction with the childbirth experience (compared to placebo). [2,3] Pharmacological choices include:

- Inhalation agents (i.e. nitrous oxide), which relieve pain compared with placebo but are associated with nausea, vomiting and dizziness [2,3]
- Systemic opioids, which are less effective than regional analgesics and frequently cause nausea and sedation [2,7]
- Local anaesthetic nerve blocks, which are especially useful for instrumental delivery and episiotomy (often in conjunction with EA) [8]
- Regional analgesia, including EA, spinal anaesthesia, and combined spinal-epidural anaesthesia (CSE)

EA is widely used for pain relief in labour and involves injection of a local anaesthetic (such as bupivacaine) into the epidural space. [2] It is typically given with an opioid such as fentanyl to limit the amount of local anaesthetic required for efficacy. This also allows the woman greater ability to bear down and push during the second stage of labour. EA effectively relieves pain (compared to opioids or placebo) but does increase the risk of instrumental delivery and caesarean section for fetal distress, and may prolong the second stage of labour by up to two hours. [2,3,9,10] Other potential adverse effects include hypotension, motor blockade, fever and urinary retention (requiring an indwelling urinary catheter). [3,7] Fear of EA side effects has been noted as a key predictor as to whether a woman will elect for EA, with one study suggesting fear of EA side effects decreases EA uptake by half. [1] As EA allows insertion of a catheter, the medication can be given by bolus injection, continuous infusion or via a patient-controlled pump. This is in contrast to spinal anaesthesia (injection of



local anaesthetic into the subarachnoid space), which, while faster and safer, does not allow insertion of a catheter for continuing analgesia. [2,10] In many centres, a combined spinal and epidural anaesthetic (CSE) is given, where a single injection of local anaesthetic is inserted into the subarachnoid space (for fast onset of pain relief) in addition to insertion of an epidural catheter for ongoing pain management. [10]

Women have widely differing views on what level of pain should be expected when giving birth. Evidence suggests that women who are more fearful of labour pain have a higher likelihood of choosing elective caesarean, and if they do choose labour, a higher chance of having an epidural. [1,6] In contrast, women who are more accepting of labour pain, and more confident in their ability to cope with it, are generally more likely to decide against EA. [1,6,11] Other personal factors that increase the likelihood of a woman choosing EA include having a previous EA, partner preference, and attending a childbirth class. [4,11] In addition, the attitudes and experiences of family and friends can influence a woman's decision. It has been shown that women with friends or family who have had positive experiences with EA are more likely to choose EA themselves. [1] Likewise, hearing stories about how excruciatingly painful childbirth is may increase anxiety about the pain and increase EA uptake for primiparous women. [1]

Looking beyond a woman's immediate circle of family and friends reveals another potential influence – celebrities and the media. There appears to be a widespread opinion (particularly amongst celebrities) that birth should be “natural”, which presumably refers to a lack of intervention. [12] Just as organic, gluten-free, paleo, and #cleaneating have taken off, a similar trend appears to be on the rise in childbirth. Perhaps next we will see the emergence of “organic” labour wards. Miranda Kerr had the media buzzing following her comments about having “a natural birth without pain relief” and not wanting a “drugged-up baby.” [13,14] Whilst it was absolutely her choice to give birth “naturally” and opt out of pain medication, her celebrity status mean that her personal experiences and opinions are likely to influence the behaviours and attitudes of women all over Australia (and potentially the world). By going out of her way to state in her official announcement of the birth of her son: “I gave birth to him naturally; without any pain medication” it infers that those who decide otherwise are making the ‘wrong’ decision. [13,14] Sweeping declarations like this have the potential to be damaging to women who did elect to use EA or needed a caesarean section. It may be that public assertions about their choices, made by Miranda Kerr and other

celebrities such as Teresa Palmer and Gisele Bündchen, have turned EA into the enemy. [12] Such statements generate significant media interest and controversy, and have led to the emergence of the term “the smug natural birth” as well as suggestions that giving birth has become “a competitive sport.”[12]

But it's not just celebrities and models that have a problem with epidurals. There is a difference of opinion between midwives and obstetricians as to how often epidural analgesia should be used. [15] An article published in *Midwifery Today* in 2010 referred to epidurals as “the drug trip of the current generation”, and even compared anaesthetists to “street drug pushers.” [16] Whilst clearly this does not represent the views of all midwives, it is concerning that a prominent publication can present these opinions as if they were fact. This article also advised it's audience of birth practitioners to remember that “a woman who can sit still long enough to have an epidural inserted during labor can have a relatively painless, unmedicated birth if she were provided adequate birth support in the home setting.”[16] This misinformation is dangerous given the fact that RANZCOG does not support the practice of planned homebirths due to its inherent and proven risks. [17] The reluctance of some midwives to offer EA has been well documented elsewhere. [15,18,19]

Furthermore, a number of Australian studies have found that the rate of epidural analgesia uptake is much higher in private hospital patients versus those seen in the public system. [20,21] A New South Wales study from 2012 reported a 40% larger uptake of EA in private hospitals compared with public, as well as an overall increase in interventions. [20] This is similar to previous Australian data reporting a 50% increase in uptake of EA in private versus public care. [21] It is clear that many women are not in a position to choose whether they receive public or private care, but nonetheless it is apparent that where one gives birth has an impact on whether an EA will be performed or not. This raises

issues of appropriate health care expenditure and a potential two-tier system in Australia that deserves adequate discussion and reflection in its own right. [20]

Ultimately, women should feel free to choose whatever pain relief they believe will help them most during labour, or to opt for none at all. Furthermore, whilst this reflection has focused primarily on women determining a birth plan in the antenatal period, women who choose non-pharmacological methods during that period should also feel free to progress to a pharmacological method during labour if they are not coping with the pain. It is important that women are informed and feel empowered to make these decisions, and this involves adequate discussion of the benefits and potential adverse effects of all their options. As the doctor – whether we are the obstetrician, the anaesthetist, the GP or perhaps even the resident, it is our job to ensure the patient fully understands that discussion. However, in order to communicate benefits and risks effectively we need an understanding of what influences a woman's choice when it comes to pain medication, even more so when attempting to navigate the controversial minefield that is childbirth. Evidence-based medicine is brilliant, but sometimes we live in an evidence bubble – so influenced by statistics that we might forget to look outside at how the opinions and actions of others can also shape our patients' decisions. To our patients, percentages may mean nothing in the face of Miranda Kerr and organic kale smoothies. A thorough discussion of a woman's fears and attitudes towards the birthing process is undoubtedly a crucial component of comprehensive antenatal care.

Conflict of interest

None declared.

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Medical Futility: The struggle to define an ancient concept in a modern clinical context

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At face value the word futility is deceptively simple, inviting synonyms such as useless, pointless, and ineffective. [1] The concept is not new, with Hippocrates espousing the importance of avoiding futile treatment measures over two thousand years ago: *"Refuse to treat those who are over-mastered by their disease, realising that in such cases medicine is powerless."* [2] It was not until the 1980s that the term "medical futility" began to receive significant attention in the medical literature. [3,4] Despite several decades of debate and hundreds of articles dedicated to the subject, the concept of medical futility remains ambiguous. [4,5] Several competing concepts and definitions have been proposed, however each of these has been subject to criticism and has ultimately failed to produce significant agreement. Increasingly, the philosophical definition of futility is proving inconsequential when applied in a clinical context. Ongoing attempts to reach a consensus distract from more significant practical issues. These include resource rationing and how best to manage conflict over patient demands for treatments that healthcare providers deem to be medically inappropriate. [5,6]

Back to basics

The Oxford Dictionary definition of futility is seemingly straightforward, defining futile as "incapable of producing any useful result; pointless". [7] Deeper consideration reveals that not only is futility by this account difficult to quantify with certainty, it is also extremely subjective and value-laden. [8] Given the capacity for humans to occasionally defy medical odds it is almost impossible to declare with complete confidence that a treatment is "incapable of producing any useful result". Ewer proposes that "in seeking a universal definition of medical futility, we may be drawing an arbitrary line in a continuum; we seek the comfortable position of declaring futility exists or does not, and we cannot always make that determination". [9] The inability to reach a universal understanding of futility despite several decades of discussion in the literature supports this assertion that futility definitions are inherently arbitrary.

Further complicating the debate is the lack of consensus as to which group of patients the concept of futility applies. Theoretically, futile treatment could be used to describe any intervention that is performed without being medically indicated. [3] Overall however, the medical literature generally considers a more limited application of futility as it applies to life-sustaining treatments. [3] Some authors argue that defining futility in the context of end-of-life measures unnecessarily clouds the debate with emotion and is partly responsible for the confusion surrounding its meaning. [10]

Paternalistic origins

While the definition of futility is often cited as the point of contention, the central issue in the futility debate is actually the authority and role of doctors in making decisions to withhold or withdraw treatment. [3] Original attempts to define medical futility aimed to provide a clear legal and ethical framework within which doctors could reasonably deny or withdraw medical therapy based solely on clinical indications for treatment, irrespective of patient preferences. [3,6] Doctors were given the power to make abstention decisions over the objections of competent patients based on their medical expertise. Unsurprisingly, this concept of medical futility drew heavy criticism on the basis that it invites medical paternalism and the imposition of doctors' personal values on patients. [3]



Physiological futility

The concept of futility was subsequently revised to that of "physiological futility". According to this definition, a futile treatment is one that is incapable of achieving its intended biological aim. [4,6] The medical expertise of doctors was still given central importance, but this definition aimed to remove subjective quality-of-life judgements from the decision-making process and provide an objective account of medical futility. [3,11] Prognostic scoring systems were touted as a means of substantiating futility assessments through empirical data. [3] The physiological futility model also drew criticism as it failed to account for individual deviations in predicted outcome (i.e. the patients that "defy the odds"). [3] Furthermore, subjective assessment still exists, as data supplied by prognostic scoring systems requires interpretation and integration with subjective evaluations to be applied to the individual patient. [3]

Quantitative and qualitative futility

Contributions by Schneiderman et al. in the early 1990s introduced the concepts of qualitative and quantitative futility into the debate. Schneiderman quantified a level at which abstention decisions could be justified, proposing that an intervention is quantitatively futile when: *"physicians conclude (either through personal experience, experiences shared with colleagues or consideration of reported empiric data) that in the last 100 cases, a medical treatment has been useless."* [12] Opposition to the quantitative futility definition (and indeed any definition based on prognostic scoring systems) centres on the idea that such definitions create "self-fulfilling prophecies". [6] If life-sustaining treatments are denied because of an anticipated high probability of death, the subsequent observed mortality rate will be artificially increased. [6]

Schneiderman went on to state that "any treatment that merely preserves permanent unconsciousness or that fails to end total dependence on intensive medical care should be regarded as nonbeneficial and, therefore, futile". [12] In proposing a quality-of-life based minimum standard against which futility could be measured the authors present the concept of qualitative futility as an alternative to quantitative futility. [3,4]

Procedural approach to futility

The procedural approach to futility moves away from semantics, focussing instead on the processes by which ethical arguments are

addressed. This emphasis on procedure over terminology emerged as it became apparent that reaching consensus on a futility definition was unrealistic. [3,4] The procedural approach promotes the establishment of processes and strategies aimed at minimising conflicts and resolving disputes related to medical futility. The utility of this method led to its adoption by a number of hospitals and endorsement by the American Medical Association [4]: *"Since definitions of futile care are value laden, universal consensus on futile care is unlikely to be achieved. Rather, the American Medical Association Council on Ethical and Judicial Affairs recommends a process-based approach to futility determinations."* [4,13] Also known as the "due process approach", this model avoids defining criteria for denying or withdrawing treatment. [6] Instead disputes around delivery of medically futile treatment are generally referred to a third party or ethics committee. [6] Unsurprisingly, this definition has also come under scrutiny for its inherent bias, as these committees are traditionally largely comprised of medical practitioners. [6]

Futility vs. rationing

Of increasing importance in the futility debate is the distinction between the terms futility and rationing. Futility questions whether a proposed treatment will work, whereas rationing questions the cost-versus-benefit of an intervention. [4] In the current health context of advancing treatment modalities and finite funding, attention is shifting away from defining futility and towards specifying a reasonable and appropriate level of care. [9]

The language of futility is also changing to reflect this shift in values towards a rationing emphasis. The Australian Medical Association supports the need to evaluate costs and benefits, stating: *"Treatment is futile when it is no longer providing a benefit to a patient, or the burdens of providing the treatment outweigh the benefits."* [14] Wilkinson et al. argue propose that "medically inappropriate" is a preferable term to futility as it makes clear the fact that it is a value judgement made by doctors and avoids the "pseudo-objectivity" conveyed by the word "futile". [6] This explanation, coupled with the procedural approach's emphasis on communication and negotiation to resolve disputes, arguably offers the most useful account of medical futility in the current health context.

A suggested approach to futility for clinicians

In the absence of a medical consensus on the definition of futility, McCabe and Storm suggest contemplating the following questions when deciding if a treatment is futile:

1. *The goal of the treatment in question*
2. *The likelihood of achieving treatment goal(s)*
3. *The risks, costs and benefits to the patient of pursuing the*

intervention, compared with the alternatives

4. *The individual needs of the patient* [15]

When doctors and patients disagree about treatment futility, the American Medical Association promotes the following seven steps to resolve the conflict:

1. *Earnest attempts should be made in advance to deliberate over and negotiate prior understandings between patient, proxy, and physician on what constitutes futile care for the patient, and what falls within acceptable limits for the physician, family, and possibly also the institution.*
2. *Joint decision-making should occur between patient or proxy and physician to the maximum extent possible.*
3. *Attempts should be made to negotiate disagreements if they arise, and to reach resolution within all parties' acceptable limits, with the assistance of consultants as appropriate.*
4. *Involvement of an institutional committee such as the ethics committee should be requested if disagreements are irresolvable.*
5. *If the institutional review supports the patient's position and the physician remains unpersuaded, transfer of care to another physician within the institution may be arranged.*
6. *If the process supports the physician's position and the patient/proxy remains unpersuaded, transfer to another institution may be sought and, if done, should be supported by the transferring and receiving institution.*
7. *If transfer is not possible, the intervention need not be offered.* [16]

Conclusion

Ultimately the definition of futility has little relevance in the current healthcare climate. With continued advances in the ability of expensive medical interventions to keep people alive, a distinction must be drawn between what *can* be done and what *should* be done. Whether it is philosophically agreeable or not, futility and rationing are inextricably linked in a practical medical sense. In the current health context, the pertinent issue is now how best to manage requests by the public for medically inappropriate treatment. Successful strategies are those that minimise conflict, promote dialogue, and shared goal setting while supporting patients and their families when the limits of care have been reached.

Conflict of interest

None declared.

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Medical humanities and narrative medicine

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Medicine is both an art and a science. While modern medical training teaches the scientific and technical aspects of medicine well, the humane aspects of medical education remain relatively neglected at university level in Australia. "Medical humanities" and "narrative medicine" have been proposed as solutions to correct this imbalance. The inter-disciplinary field of "medical humanities" brings the perspectives of academic disciplines within the humanities to bear on medical practice. "Narrative medicine" teaches us how to hear our patients' stories and how to respond to them. These approaches provide crucial opportunities to develop attention to narrative, critical thinking and empathy, and thus to deploy the scientific tools of medicine more wisely.

"The art of tending to the sick is as old as humanity itself."

– Goldman Cecil's Medicine [1]

The practice of medicine is both an art and a science. Both aspects require due attention, but throughout my university medical training it always seemed clear that scientific and technical topics were considered more important. After all, they received the majority of attention in the curriculum, and were more thoroughly examined. Important topics such as bioethics, social determinants of health, and the history and philosophy of medicine were balanced precariously at the periphery of our studies or even absent from the core curriculum.

Modern medical training emphasizes the scientific, technical and practical. Although patient communication, empathy and professionalism are rightfully given prominent places in modern medical school curricula, these are approached in typically pragmatic fashion – for example, how might one convey the impression of interest to a patient? We learn how to sit, how often to nod, when to make eye contact, and what we might say to appear to be listening. The evidence of my patient communication tutorials is scribbled in the margin of my first year textbook: "I see ...", "please go on ...", and "mm-mm ...". We learn this by rote, like everything else. This is an excellent place to start. But why bother at all? Mostly, we talk in terms of establishing rapport, taking better medical histories and improving the end results for our patients. However we never discussed the bigger questions that underlie all this effort to appear caring, for example, how to stimulate and sustain genuine interest in the endless stream of people we will meet as patients, let alone why we seek to relieve suffering or value human life at all.

From my own experience as a student, peer reviewing reflective essays or participating in tutorial discussions, the result of this heavily unbalanced emphasis is that medical students think no more subtly about important ethical issues in medicine than the typically hackneyed discussions one reads in the newspapers. This is despite our experiences with doctors and patients everyday in clinic and hospitals, for whom these are not abstract issues. For example, when discussing dilemmas encountered by doctors who are religious, someone may always be relied upon to pipe up with the peculiar remark that doctors ought to leave their personal values at home and not bring them to work – as if the doctor with no values was anything other than monstrous to contemplate. Why aren't we able to transform this abundance of clinical experiences into better thinking on "big" questions? This mediocrity in critical thinking and imagination is dangerous for both our future patients and ourselves. However, the issue is larger than



simply a lack of time for bioethics in the curriculum. The loss of space in the curriculum for this endeavor is but one manifestation of the lack of importance accorded to the humanities as a whole in medical training.

"Medical humanities" and "narrative medicine" have proposed themselves as solutions to this lack of the humane in modern medicine, to balance its increasing focus on the reductionist and scientifically technical. [2-3] Here I address the question of what it means to recover the sense of our profession as a humane art, especially via narrative medicine.

What are the medical humanities and narrative medicine?

Training in narrative medicine and medical humanities now forms part of the core curriculum at more than half of all North American medical schools. [4] However, despite the considerable influence of these fields in Europe and America, the concepts remain little known in Australia. "Medical humanities" refers to the interdisciplinary fields created when the perspectives of the humanities, social sciences and the arts, such as literature, history, music, languages, theology and fine art are brought to bear on medical practice and other areas relevant to healthcare. [5]

"Narrative medicine" in turn belongs within the wider field of the medical humanities. It is more than simply the observation that patients and their illnesses have stories, but this simple statement is where it all begins. The field of narrative medicine grew out of the work of physician Rita Charon who formally defined "narrative medicine" as medicine practised with "narrative competence", that is, "competence to recognize, interpret, and be moved to action by the predicaments of others". [6] Elsewhere, Charon describes narrative medicine more simply as "medicine practised by someone who knows what to do with stories". [7] Training of medical professionals in this field teaches the application of formal literary theory and creative writing skills to the situations and interactions commonly encountered in medicine, as well as various interpersonal skills. To this end, the narrative medicine program directed by Charon at Columbia University trains participants in "close reading, attentive listening, reflective writing, and bearing witness to suffering". [7]

One way of understanding about how to "do" narrative medicine is conceived in terms of three "movements" – attention, representation and affiliation. [7] Attention refers to the skill, when in the presence of

our patients, of absorbing as much as possible about their condition. We recognize this as what we do during the observation phase of physical examination, for example. Representation refers to the act of writing about patients and our clinical experiences, “taking chaotic or formless experiences and conferring form”, for example as prose or poetry, a piece of written dialogue, or even as an obituary. This process creates meaning from our experiences. Finally, affiliation refers to “authentic ... connections between doctor and patient”.

First movement: attention

Observation is the first step in any medical examination, and all-too easily overlooked when one is learning. All medical students soon develop some favourite trick for overacting this step during OSCEs, to impress our keen skills of observation upon the examiners. But how is one really to develop this skill? The obvious answer is by practice and experience with observation of real patients on the wards – learning to see the walking aids, asthma puffers, sputum containers, hearing aids and every other manner of salient item in the jumble of medical equipment and personal items at the patient’s bedside.

However, it is also possible to practice the skills required for observation in medical contexts in other settings, such as art galleries and museums. This approach was developed at U.S. medical schools, to teach skills such as objective observation, communication, disagreeing respectfully with peers and managing ambiguity. At the University of Melbourne, a method first developed at Harvard University (“Training the Eye”) is being used at the university’s Ian Potter art gallery for improving the observation skills of medical and dental students. [8] This program is based on the hypothesis that the process of understanding a complex, narrative-based painting requires many of the same skills as required for medical diagnosis. Access to this training is not routine for medical students, but can be sought out in elective sessions at the medical school’s annual student conference. In one such session, we used the wonderfully intriguing painting “Bushrangers”, painted by William Strutt in 1852. It is not immediately clear that the painting involves a highway robbery in what is now downtown St Kilda in Melbourne; drawing this inference requires deliberate searching through the painting’s details and debate about the significance of aspects of the painting with others. This approach has been shown substantially to improve the observation skills of medical students. [9] It is useful not only for observing our patients, but for a variety of other situations, such as understanding medical imaging and communicating our findings to colleagues and patients.

Second movement: representation

A crucial aspect of narrative medicine is learning to write about one’s practice and patients. Opportunities to develop this skill begin during medical school with reflective writing exercises about our clinical experiences and patient encounters. Another way to improve one’s own writing, apart from regular practice through reflective writing, is to read published examples of this kind of writing, of which endless excellent examples by both doctors and patients are available.

The genres of narrative medicine have been classified in various ways. One simple classification recognizes four different genres. [10] Firstly, there are the classic illness narratives that patients write about being sick, and which might include surrounding circumstances explaining how they were diagnosed, how they were treated, how they coped and the impact it had on them and their families. An excellent, recent Australian contribution to this genre is Myfanwy and Donald Horne’s experience of Donald’s palliative care for chronic obstructive pulmonary disease (COPD), and the aftermath, chronicled in, “Dying: a memoir”. [11] Helen Garner’s “Spare Room” is an interesting Australian variation on the patient memoir, written from the perspective of a concerned friend. [12] “The diving bell and the butterfly”, Jean-Dominique Bauby’s compelling memoir of locked-in syndrome, is a classic in the genre. [13]

Secondly, many doctors write about their experiences of caring for

their patients. Many will be familiar with the thoughtful writing of the Melbourne-based oncologist, Ranjana Srivastava, both in her regular newspaper column and her books, such as “Tell me the truth: conversations with my patients about life and death.” [14] The delightful books of Oliver Sacks, detailing the curious cases he encountered in his long practice as a neurologist, such as “The man who mistook his wife for a hat” also belong within this genre. [15] “The hospital by the river: a story of hope” by Catherine Hamlin about establishing the Ethiopian fistula hospital with her husband is a must-read for Australian medical students [16]; I found a copy on the midwives’ shelves during my obstetrics term and read it late at night between calls to labour suite. There are memoirs at all level of practice; the notorious memoir of life as a junior doctor in an American hospital, “House of God”, is by now legendary, along with its questionable additions to the medical vocabulary. [17]

Thirdly, there are doctor-patient narratives. These are narratives which show how not only the patient’s perspective on their illness, but also how their experience of illness was affected by the interaction with their doctor. These make us aware of how our reactions to patients and explanations of their symptoms can affect a patient’s understanding and experience of their illness. These narratives form in the interplay between doctor and patient in the taking a history, and in forming a diagnosis. Both the doctor and patient will begin to form stories about the illness in this process, which will necessarily be changed by the therapeutic encounter. This might be observed, for instance, when a newly diagnosed patient commonly asks whether anything might have been done to prevent their illness – did they do something to cause it – are they somehow to blame?

Lastly, we need to be aware of meta-narratives, which are the grand, over-arching stories our societies and cultures tell about illness and health, and which provide a framework within which we conceive and construct our own stories. A classic work in this area is Susan Sontag’s seminal “Illness as metaphor”, which examines the power of metaphor and myth in cancer, and was written during her own experience (we will not say “battle”) with cancer. [18] Arthur Frank’s “The Wounded Storyteller” is likewise a seminal text, as a collection of essays discussing the roles and limitations of different categories of illness narratives, and written in light of the author’s own experience of serious illness. [19] Jonathon Miller, although understandably better known for his influential stage production of Gilbert and Sullivan’s *The Mikado* starring an operetta-singing Eric Idle as Ko-Ko, was also a neurologist. His multi-series documentary and book “The body in question” is another influential endeavor in the genre of medical metanarrative, dealing as it does with metaphors of illness, and cultural ideas about the body. [20]

Third movement: affiliation

How then does one “do” narrative medicine in daily medical practice? The most important element in building the required therapeutic affiliation with patients in narrative medicine is “a specific openness to towards patients and their narratives”. [10] Charon notes that when she began to try this approach with her own patients, she asked only one question during the initial consultation: “I have to learn as much as I can about [your] health. Could you tell me whatever you think I should know about your situation?”. [21] While most of us would worry about the extra time it would take in a consultation if patients were allowed to speak without direction, one study showed that two minutes was long enough in General Practice for 80% of patients to explain all of their concerns, if the doctor was trained in active listening and even if the patients had complex medical concerns. [10] Nevertheless, ensuring that a consultation with a patient “meets both narrative and normative requirements” is unquestionably difficult and requires training and daily practice. [22]

Proponents of narrative medicine argue that literature is an important way to develop the narrative mindset for medical practice of this kind. The touted benefits to doctors of reading “good books” include that

reading offers a wider experience of life than one may encounter in the everyday of a single lifetime. [23] The narrative perspective, it is claimed, also has the potential to develop the imagination on which empathy depends, by crossing barriers into the inner lives of others in a way that is not possible in real life, even with the unique insights into others' lives provided by medical practice. [23] It is also said that literature can also refine moral perception, and teach one to manage with ambiguity and paradox. [24] However, despite these optimistic expectations, medical students have proven resistant to the projected benefits of reading for this purpose. The obviously frustrated authors of one study document students refusing to participate in their carefully prepared class ("the literature we selected would have made Tolstoy proud"). They had hoped to discuss passages from novels covering themes such as illness, family violence race, gender, social class and sexual identity. [25] The students responded in a way that will be familiar to any of us who have attended classes on topics commonly deemed by the student body to be "fluffy" – questioning the basis of the class, not taking it seriously, treating presenters with disrespect and even not attending the class. Some of this resistance is laudable – the impatience of the practically-minded for weasel words and time wasting, and a weariness with endless jostling to advertise various medico-political agenda within our curriculum. However, it is also likely that the resistance arose, as the authors suggested, from a refusal to persist with uncomfortable topics which also ask a group of students who see themselves as triumphant meritocrats to reflect on the undeserved social advantages that have enabled them to study medicine at all.

Conclusion

Much has been claimed for the benefits of narrative medicine. However, writers in the field caution against over emphasizing the artificial dichotomies of humanities versus the sciences, the subjective versus the objective, the clinical and reductionist versus the human and holistic. [26,27] Competent medical practice necessarily requires compassion and imagination, and cannot avoid "big" questions such as the nature and meaning of pain, suffering and death. However, a doctor who is able to respond usefully to these fundamental questions requires training and skills beyond the merely technical and scientific. Other potential benefits suggested for this approach include the preservation of empathy throughout medical training, reduced doctor burnout, exhaustion and disillusionment, and better outcomes for our patients. [4]

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How can we learn narrative medicine? At medical school, this might be about making time to read widely and explicitly resisting the pressures towards reductionism and technical focus. Another important way to preserve and develop narrative sensibilities is by writing about our own clinical experiences and patients. An obvious example in this respect is simply to take reflective writing opportunities seriously, and to expect high standards of writing from others when asked to give peer feedback. For junior doctors, opportunities for joining Balint groups at hospitals or during GP training are also becoming more widespread. These small groups meet to present and discuss cases from members' own practice, with focus on narrative, the doctor-patient relationship, and self-reflection. [28] However, the options in Australia for formal academic training in the humanities, as a medical student or doctor, are limited. The only explicit university program in medical humanities in Australia is at the University of Sydney, which offers "health humanities" as a specialization in the Masters or Graduate Diploma of Bioethics. [29] Another option is attendance at shorter workshops that overseas institutions offer from time to time, and which we might seek out during study leave. The most well-established of these are those offered at mid-year at the University of Columbia Medical Center in the U.S. [30]

Medicine practiced without attention to the humane has the potential to harm both our patients and ourselves. While science provides us with safe, effective tools to deploy in medical practice, the humanities teach us how to use them wisely. [31] Currently, university medical training focuses on the former, with limited opportunities to develop the attention to narrative, critical thinking and empathy which help us to develop wisdom in response to clinical experience. Oliver Sacks summarizes this aptly, "With the rise of technological medicine and all its wonders, it is equally important to preserve the personal narrative, to see every patient as a unique being with his own history and strategies for adapting and surviving. Though the technical terms may evolve and change, the phenomenology of human sickness and health remains fairly constant ..." [15]

Conflict of interest

None declared.

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So You want to be a Haematologist?

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Introduction

Discussion surrounding specialties of preference is commonplace in medical school, across all levels of training. Some are attracted to the breadth of care afforded in general practice, the in-depth expertise of organ systems in physician specialties, or the hands-on experience with human anatomy in surgery. A few of us however, appreciate the opportunity to care for patients by the bedside, followed by investigating their bodily samples under the microscope in search of an answer to their presenting problems.

Belonging to the last group, I present this article which summarises my elective term experiences in haematology at the Olivia Newton-John Cancer & Wellness Centre and the Guy's Hospital. This, I hope, will shed some light on haematology as a potential field of interest for medical students – one that many of us consider 'exotic' and thus, perhaps, less pursued.

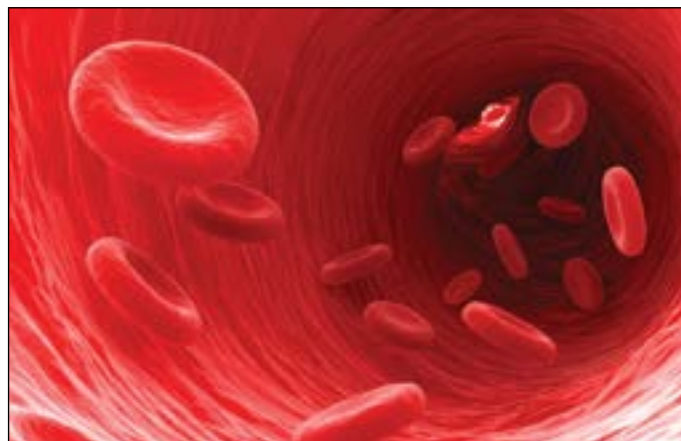
Haematology – what's in a specialty?

Haematology is an integrated discipline that incorporates both clinical and laboratory skills to diagnose and treat diseases of the blood and blood-forming (haematopoietic) organs. [1] The blood's cellular components include the red blood cells, white blood cells and platelets, which are derived from the bone marrow in steady-state conditions. Extra-medullary haemopoiesis in the liver and the spleen occurs in certain disease states, for example in marrow failure syndromes and haemoglobinopathies. In addition, the coagulation factors, which assist clotting, are also an important part of the haematological system. Principally, haematologists treat disorders which arise from derangement of any of these blood components – too high, too low or dysfunctional – as a result of diverse pathological processes, broadly classified as malignant or non-malignant. [2]

Clinical exposure and latest research

To set the scene, my first placement took place at the Olivia Newton-John Cancer & Wellness Centre in Melbourne. A new addition to the Austin Health complex in 2013, it is a comprehensive cancer centre which offers a holistic approach to patient care. On top of routine inpatient and outpatient services, the Olivia Newton-John Cancer & Wellness Centre provides a range of wellness therapies, such as music therapy, art therapy and massage. [3] Following a short vacation, I then set off to London, where I undertook my second placement at the Guy's Hospital, a major teaching hospital affiliated with King's College London. Located in Central London, this is the hospital where Thomas Hodgkin once worked. [4] I would like to share interesting current trends in clinical haematology I came across whilst on this placement.

At the Guy's Hospital, I was privileged to work with the Myeloproliferative Neoplasms (MPN) Unit, an internationally renowned centre for the care of patients with MPN spectrum: polycythaemia vera, essential thrombocythemia, and primary myelofibrosis. The MPN are characterized by clonal proliferation of myeloid progenitor cells in the bone marrow and in many cases, liver and spleen. [2] The advent of rapid genome-wide sequencing has identified a number of important mutations responsible for these disorders, including mutations in the Janus kinase 2 (JAK2), the MPL proto-oncogene, thrombopoietin receptor (MPL), and most recently the calreticulin (CAL-R) genes. [5] A particularly important 'newcomer' for MPN treatment I encountered there was ruxolitinib, a JAK1/2 inhibitor, which has been licensed for



primary myelofibrosis since the landmark publication by Prof. Claire Harrison in 2012. [6] This paper demonstrates superior efficacy of ruxolitinib compared to conventional therapy (usually hydroxyurea), in improving splenomegaly and overall quality of life. In addition, there is some evidence that ruxolitinib may also improve survival in patients with primary myelofibrosis, although this needs to be further investigated. [7] Witnessing patients' experiences first hand in her MPN clinics was a fantastic experience; especially given the limited efficacy and increased complications experienced with hydroxyurea. [6] At the moment, the Guy's Hospital and other centres of excellence in the UK and Europe are running further clinical trials assessing the use of ruxolitinib in polycythemia vera, with promising results reported in a recent study. [8] With corroborative studies, it is anticipated that ruxolitinib will be incorporated into the standard of care for patients with polycythemia vera as well.

On the other hand, I spent most of my placement time at the Olivia Newton-John Cancer & Wellness Centre on ward service. An important lesson I took away is the clinical care of serious infections in haematology patients. Febrile neutropenia is the most common and important infective issue suffered by up to 80% of neutropenic patients with haematological malignancies on chemotherapy. [9,10] Primary haematological disease, along with high-dose chemotherapy, results in profound neutropenia, putting patients at risk of invasive bacterial infections. Compounding this risk is chemotherapy-induced gastrointestinal damage, which allows for translocation of enteric bacteria into the blood, causing bloodstream infections. [11] In particular, bloodstream infections with the extended-spectrum beta-lactamase and the carbapenemase-producing Gram-negative bacteria pose significant issues as these pathogens are resistant to empirical therapy for febrile neutropenia (which is commonly a broad-spectrum cephalosporin-based regimen with an anti-pseudomonal cover). [12] Increased mortality risk with these multi-resistant organisms is related to delays in delivering appropriate antibiotic therapy. [13] Indeed, we observed one case of bloodstream infection caused by an extended-spectrum beta-lactamase producing Gram negative bacteria, in which the patient remained febrile after a period of empirical therapy with piperacillin/tazobactam, prompting the switch to a carbapenem-based therapy, allowing an adequate antimicrobial cover (luckily the isolate did not harbor a carbapenemase-producing bacteria as well). Antimicrobial stewardship and adequate infection control measures are required to prevent further problems with multi-resistant

organisms, which has been an initiative worldwide today, including in Australia. [14]

Reflections on the elective placements

An elective placement will not be complete without reflecting on what I have learnt whilst there to make me a better doctor in the future.

First, I have come to truly appreciate the importance of research in clinical medicine. Research, both laboratory-based and clinical, provides the essential foundation of what we know at present of diseases and their appropriate management. As an intern candidate sitting interviews in two months time, the way I view my research involvement has been affirmed – it is no longer merely a ‘selling point’ in my *curriculum vitae*, rather it is something I am truly proud of – it is a contribution to humanity which I certainly would like to keep up. Haematology, in particular, is a very active field of scientific enquiry. In both centres I attended, there are numerous clinical trials that are still actively recruiting patients at the time this article is written. In recent years, ‘targeted therapy’ and ‘immunotherapy’ have taken the centre stage and my experience with ruxolitinib described above is one example.

Secondly, good communication skills are crucial for best patient care, especially in haematology. In such a discipline with high throughput of novel, potentially superior therapy, at times quality of life may be neglected (unintentionally) for ‘overall survival’, which is often used as a measure of treatment success. A career in haematology hence requires the ability of not only to offer hope via new therapy, but also to limit further suffering by the same token. Taking the time to empathically listen to patients’ wishes is very important, along with careful considerations on the potential benefit and side effects of the therapy on offer.

The natural history of malignant haematological disorders often alternates between periods of remission and relapse – at which a new treatment modality is usually offered. However, it is not uncommon that these ‘salvage therapies’ are offered on a clinical trial basis, where there is an uncertainty of whether or not we are doing more good than harm. Numerous times I had observed careful, empathetic listening followed by the question ‘is this what you really want?’ which revealed the true desire of our patients – that they prefer to embrace the time that remains free of side effects (nausea and fatigue are common ones) and are able to treasure their loved ones with minimal medical interventions. In such cases, close liaison with palliative care services is crucial in ensuring that we always act in our patient’s best interest. Having learnt this firsthand observing the consultants I had worked with in my electives, I most certainly will remember to put my patients’ (true) wishes first in my future practice.

So you want to be a haematologist (in Australia)?

There are three training pathways available in the Australian system (Figure 1). I will briefly discuss the joint RACP/RCPA training pathway here as it is the most commonly chosen pathway, and was the only pathway the registrars I worked with had undertaken. [15]

After completing their Basic Physician Training (BPT) program, candidates are eligible to apply for the joint RACP/RCPA accreditation in haematology. This involves the completion of four years of advanced training in haematology, usually comprised of two years each of clinical and laboratory training (minimum requirements of two years and one

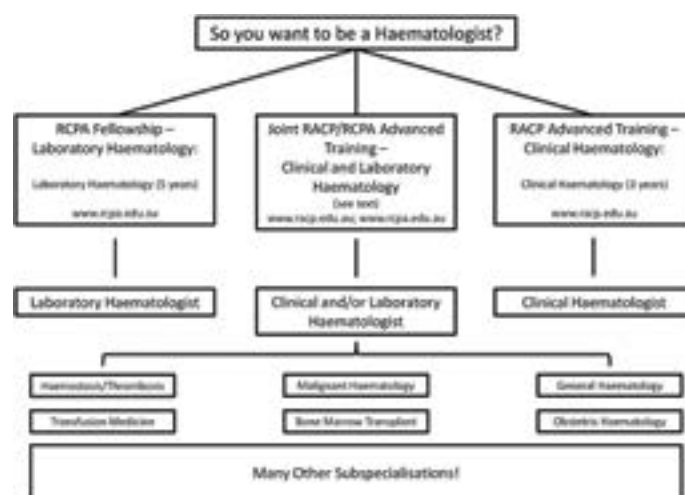


Figure 1. Haematology Training Pathways in Australia. Haematology affords a wide range of career options and subspecialties depicted here are by no means exhaustive. Please refer to www.racp.edu.au and www.rcpa.edu.au for a comprehensive overview of these training pathways.

year in laboratory and clinical haematology training, respectively). [15]

In addition to the RACP written and clinical examinations taken in the final year of BPT, joint accreditation trainees are required to complete the RCPA haematology part I and part II pathology examinations after at least 18 months of accredited laboratory training. [15] The part I examination includes written, morphology, ‘wet’ and ‘dry’ practical examinations plus a viva, while the part II examination includes a dissertation and a viva. Hence, those considering haematology as a vocation should take this component of the training into consideration – there will be pathology exams!

Pathways that follow to ‘consultanthood’ vary, with many fledgling haematologists pursuing further training through fellowship appointments or a Doctor of Philosophy degree (PhD). As a result, haematology affords a wide range of career destinations and many subspecialisations (Figure 1). Those who choose to work as a clinical haematologist provides inpatient and outpatient care, whilst laboratory haematologists hold supervisory role in accredited laboratories. Finally, private practice is also very common in Haematology, allowing for flexibility in matching vocational aspirations with personal pursuits.

For a more comprehensive overview of these training programs, please refer to the RACP (www.racp.edu.au) and RCPA (www.rcpa.edu.au) websites.

In summary, haematology is an attractive specialty as in many cases the haematologist has the satisfaction of seeing a patient clinically, making a diagnosis by looking at his/her patient’s blood and finally, offering appropriate treatments. Aligned with a previously published British article by O’Connor and Townsend [16], I think we agree that Haematology is, definitely, a specialty worthy of consideration.

Conflict of Interest

None declared.

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Saving behaviour cleans hands: A reflection on the behavioural psychology of hand hygiene

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As a Christian, Raelene longs to make a difference where it is most needed. With a passion for global health, she dreams to serve in tropical and remote populations of Australia and around the world. Tropical infections such as melioidosis, tuberculosis, and malaria have particularly fascinated her. She has also had a growing interest in psychology and mental health. Raelene is currently in her fifth year of medicine, planning to begin a Masters of Public Health and Tropical Medicine in 2016 and hopes to be accepted into the Rural Generalist Internship Program at Townsville Hospital.

Introduction

Since the time of Semmelweis, it has long been realised that hands are the commonest vehicles for the spread of hospital-acquired infections (HAI). If all transmission opportunities, as defined by the World Health Organisation (WHO), were met with proper hand hygiene, the current incidence of HAIs could reduce by more than half. [1-3] Unfortunately, almost every hospital fails at this. Globally, the diverse roots of noncompliance in healthcare workers (HCWs) need to be tackled in a multifactorial way. Lack of resources, high-intensity workloads and ignorance about hand hygiene necessity or technique are often first to be blamed and rightly so, according to large studies in multiple countries. [4-6] However, in most Australian hospitals where regularly-replenished hand hygiene products sit at every bedside and informative posters are abound on corridor walls, compliance still remains at 82.2%. [7] Ajzen's Theory of Planned Behaviour (TPB) proposes that it is not only the factors external to the individual, such as those aforementioned, but also internal behavioural factors that shape an individual's hand hygiene practices. [8] These internal factors, often less explored than external factors, will be the topic of discussion.

Centrality of intention

The central thesis of TPB is this: the likelihood of performing a voluntary behaviour is best predicted by the *intention* to do it. [8] According to Ajzen, intention is the extent of effort one is willing to go to in order to achieve that action. [8] A 2012 Cochrane review and a landmark hand hygiene behavioural study by O'Boyle et al. demonstrates this positive association between intention and behavioural achievement. [15,16] Even so, it is imperative early in this discussion that we not assume that self-reported scores are good measures of actual compliance; in reality, the association is demonstrably poor because external factors do commonly prevent intention from actualising as behaviour. [15,17] However, external factors are not the focus here.

Intention is determined by three secondary internal factors – attitude, social norm and perceived behavioural control – that are, in turn, a function of beliefs based on one's information about a behaviour. [14] We will now explore these factors in detail.

Attitude

Attitudes derive from an individual's cognitive and emotional evaluation of behaviour. This evaluation, in turn, depends on the various positive or negative attributes and consequences the individual has associated with the behaviour. If HCWs perceive positive attributes about hand hygiene, the desirable attitudes this yields increases their levels of intention and correlate well with compliance. [6,14,15] One's perceptions hinge on one's beliefs about a behaviour. [14,15] Based on a focus group study of 754 nurses and a 2006 review, beliefs about hand hygiene can originate inherently or electively and account for 64% and 76%, respectively, of variation in intention. [18]

Inherent beliefs

During most individuals' childhoods, exposure of hands to 'dirtiness' becomes ritualised as a trigger for disgust and the subsequent urge to cleanse one's hands. Consequently, inherent patterns develop. [18-20] The toilet-training years may see a solidification of positive attitudes towards hand hygiene behaviours specifically in situations



where individuals feel the instinctual need to 'emotionally cleanse' themselves. [18] This positive association appears consistent across diverse demographic groups. [21] However, what varies is each individual's tolerance threshold of contamination before they feel the urge to cleanse, in accordance with culture, exposure to education and environment. [1] The 500 Australian respondents to a 2008 international hygiene beliefs survey on average scored one of the lowest levels of concern about "getting sick because of poor hygiene" and "being infected in contact with other people". [22] Yet, a similar survey found that Australians do still place a strong emphasis on handwashing. [23] In reality, the hand hygiene standards promoted by Australian culture in general may be suboptimal to what is actually required for microbiological protection. It is common for nurses to only feel compelled to wash their hands after becoming 'emotionally soiled' from touching patients' axillae, groins, genitals or excretions, if visibly contaminated, or from feeling moist or gritty, but not in other situations. [18] Although long-standing, developmentally-based inherent beliefs about dirtiness are possibly the most challenging of the psychological factors to address, one intervention could be the incorporation of emotionally evocative themes and slogans in infection control campaigns.

Compliance figures also suffer when the inherent belief associating hand hygiene with self-protection is undermined by products that have caused users pain, discomfort and/or the occasional hypersensitivity reaction. With the transition to the standardised use of emollient-containing alcohol-based handrubs (ABHR) across Australian healthcare facilities since 2008, the skin damage, irritation and dryness associated with handwashing with soap have dramatically reduced. [24-26] Although the addition of emollients to the ABHR solutions has greatly reduced associated stinging sensations and contact dermatitis, ABHRs remain painful to use for some, most likely due to improper use, having split or cracked skin, or allergic dermatitis. [26] Whatever the reason, the formation of new inherent beliefs that emotionally link pain and discomfort with correct hand hygiene behaviour continually works to worsen behavioural compliance. [1,27] It seems the only way to address this problem is to await advances in dermatological products in order to further enhance the dermal tolerance of ABHRs.

Elective beliefs

On the other hand, elective attitudes originate from beliefs that deliver the schema of hand hygiene over to choice. Elective beliefs measure various hand hygiene behaviours according to a less intuitive outcome of a higher order – microbiological self-protection proved by objective laboratory evidence. The opportunities for hand hygiene just after HCWs touch ‘emotionally clean’ parts of patients or inanimate surroundings, autoclaved equipment, hospital telephones or computers are the key targets of these elective beliefs. [18] Inherent disgust alone cannot be relied upon to stimulate enough intention in HCWs to engage in appropriate disinfection during these situations. Indeed, it is no surprise that hand hygiene opportunities that specifically relate to elective beliefs are the ones most frequently neglected by nurses, especially during peaks in workload. [18]

It seems the solution is not as simple as correcting inaccurate elective beliefs. In contrast with the way inherent beliefs naturally permeate one’s attitudes, translating elective beliefs into attitudes is often met with resistance. [18] Although the best targets for change would be unique for every HCW, some common determinants affecting elective belief-to-attitude translation have been identified. Firstly, elective beliefs regarding hand hygiene opportunities at work also tend to mirror hygiene beliefs about corresponding out-of-hospital situations. The more concerned a HCW is about handwashing before preparing a meal or after stroking pets or using a computer, the more likely they are to have positive attitudes about using the proper hand hygiene after ‘emotionally clean’ events at work. [18] Notably, the previously mentioned 2008 hygiene beliefs survey demonstrated Australians were amongst those who expressed the lowest concern for “hand hygiene while cooking and eating”. [22] Perhaps, infection control campaigns could be made more effective by challenging the household habits and beliefs of HCWs in addition to their usual chastisements targeting scenarios within the work context.

Secondly, although this subject requires further research, religious attitudes concerning hand cleansing rituals could also influence the elective beliefs of Buddhist, Hindu, Muslim and Orthodox Jewish HCWs. They are encouraged, if not commanded, to clean their hands for hygiene, usually following ‘unclean’ acts and meals. [1] Additionally, having a community-oriented mindset in favour of protecting others would also strengthen positive attitudes towards hand hygiene. [1] Although less than 7.3% of the Australian population affiliate with these religions and much of Western society tends towards individualistic ideals, [28] these findings could assist local campaigns in areas where there are more individuals within these target groups, for example, at hospitals located in culturally and linguistically diverse suburbs.

Lastly, a more modifiable aspect of elective beliefs that could strengthen good attitudes is having a solid understanding of the scientific evidence proving the microbiological protectiveness of hand hygiene. [20] Most awareness campaigns rely heavily on the positive association between good knowledge, belief in the strong efficacy of hand hygiene practices, and compliance. [1] The Australian National Hand Hygiene Initiative recommends “evidence-based education on all aspects of hand hygiene in healthcare” for student HCWs, and for local initiatives to help HCWs “understand the evidence underlying the recommendation” to use ABHRs. [29]

The evidence is up-to-date and irrefutable, the studies too countless to ignore. Proper hand hygiene curtails HAI rates dramatically. [3,30-38] Yet, despite awareness campaigns and convenient online access to the major literature, HCWs (mostly in developed nations) still cite the lack of convincing evidence as their reason for non-compliance. [18,20] There are several common reasons for this. The evidence base does lack randomised controlled trials (RCTs) that are hospital-based and double-blinded. However, such studies are unfeasible; it is impossible to blind subjects from their own hand hygiene practices, implementing a control group would clearly be unethical to patients, and it is extremely difficult to simulate a realistic hospital working environment (the lack of which may confound results). [39] Nevertheless, ample community-based

open RCTs and cluster trials have produced sufficiently convincing, high-quality results. [40-44] Another common objection blames ABHRs for increasing the incidence of *Clostridium difficile*-associated diseases. However, this has long been epidemiologically refuted. [1,32,45-49] Perhaps the deepest reason why it is not sufficient to simply educate HCWs about the evidence of the benefits to patients is this – being convinced about the *self*-protective efficacy of elective hand hygiene motivates many HCWs much more than knowing its *patient*-protective efficacy does. This attitude has been a recurrent finding across the various age groups, levels of employment experience and backgrounds of scientific training. [18,20] It may do well for awareness campaigns to place even greater emphasis on evidence demonstrating the self-protective nature of hand hygiene.

Subjective norm

The second determinant of intention is subjective norm – the perception of how positively hand hygiene is endorsed by the people one respects within the workplace. [15,50] Staff members viewed as role models have the greatest impact on a HCW’s subjective norm. In 2009, Erasmus et al. conducted focus group studies on 65 nurses, consultants, junior house officers and medical students across five hospitals. Although their study was Netherlands-based, Erasmus et al.’s analysis of the social norm dynamics occurring within a hospital environment still offers key insights into the interplay between subjective norms and compliance for Australian HCWs. The study subjects most commonly identified doctors and experienced nurses, such as nurse managers, as their role models for clinical practice. [20] Another study also identified hospital administrators as role models. [18] At a busy neonatal intensive care unit, staff intention to practise good hand hygiene significantly increased when senior staff members’ opinions on the practice were perceived to be more favourable. [51] Thus, mass improvement could be found in encouraging the role models of each workplace to be thoughtful in their speech, ideas and habits, especially when around their colleagues.

Conversely, Erasmus et al. also highlighted how negative role models have the greatest power over medical students and junior nurses. [20] Perhaps this is because junior members of the healthcare team are frequently the most sensitive and feel that their behavioural control (explored in the next section) is being limited whenever subjective norms are defined by negative role models. [52] For example, in the study, many medical students believed they were unable to satisfactorily disinfect their hands between seeing patients on ward rounds because they would otherwise fall behind the rest of the team. Furthermore, in attempts to assimilate into their working environments, students admitted to imitating hospital staff, particularly doctors, without questioning their actions first. These findings demonstrate how the cycle of noncompliance could persist from one generation of role models to the next. [20] It is possible that the pressure on students to imitate senior HCWs could arise from the heuristic method of teaching common in medical schools, as well as the professional expectation that senior doctors mentor junior doctors. Being encouraged to learn from supervisors opportunistically, students often slip into the habit of accepting all advice unfiltered. Students may benefit from being regularly reminded of this pitfall by their clinical preceptors.

Peer HCWs, although not role models, may also degrade subjective norms in a hospital by contributing to its ‘culture’ of noncompliance. A negative subjective norm rooted in so widespread an acceptance of noncompliance can inform the elective beliefs and attitudes of less-experienced HCWs who may be more vulnerable to believing whatever they observe to be correct. [20] A cross-sectional survey of 2961 staff revealed that doctors and nurses experienced a strong direct association between intention and peer pressure from within their own respective professions. [53]

There have been many interventional attempts to nurture a culture of compliance. Many Australian hospitals have designated ‘hand hygiene champions’ as culture-enforcers and role models. Infection

Internal factor	Problem	Suggested intervention
Attitude – inherent beliefs	Long-standing concepts of emotional dirtiness excludes many situations where hand hygiene is actually imperative	Make campaign slogans emotionally evocative about dirtiness.
Attitude – elective beliefs	Out-of-hospital elective beliefs may translate into poor in-hospital practices	Stimulate thought about household habits and beliefs outside of work.
	Religious beliefs and community mindset	Where applicable for the audience, draw on the ways their religious beliefs support good hand hygiene.
	Misconceptions about scientific evidence	Emphasise evidence for the self-protective nature of hand hygiene, as opposed to mainly focussing on evidence of patient protection.
Subjective norm	Poor role modelling by respected HCWs	Encourage thoughtful practice in the role models of each workplace.
	Blind imitation of poor role models	Clinical preceptors could remind students of this pitfall.
Perceived behavioural control	Lack of self-efficacy	Increase HCWs' confidence in practising what they have already learnt.
	Feeling constrained by time restrictions or overbearing opinions of senior staff	Foster assertiveness and knowledge about hospital policy regarding patient safety. Practise escalating concerns with other staff.

Table 1. Summary of possible interventions

control teams design encouraging posters and use frequent audits with feedback to staff in attempts to stimulate inter-ward competitiveness and a sense of shared responsibility about compliance. However, a subculture of resistance to these strategies has emerged. [54] It is not uncommon to hear staff comment with an undertone of rebellion, “I wash my hands for extra long when the infection control police are around.”

Perceived behavioural control

The third independent determinant of intention, perceived behavioural control, describes one's *self-perceived* likelihood of performing an action. [15,51] As part of a focus group study, Australian nurses identified the most common external influences on their control over hand hygiene performance. Many felt they lacked the relevant training in infection control. They reported that regular education programs and simple “Five Moments” charts placed around wards would avert any growing misconceptions about the need for disinfection after touching patient surroundings and remind them when they forget or get distracted. [55] During peaks in busyness or emergencies, HCWs have also indicated having no time to adhere to every moment of hand hygiene. Other times, when in the middle of performing certain tasks, they may feel unable to interrupt the activity to go clean their hands midway. Lastly, disapproval of hand hygiene by senior staff, mostly doctors, was discussed as a salient issue in focus group studies. All these factors were negatively associated with intention, measured by self-reported compliance. [6,20,53,55,56]

There is an important distinction between one's perceived control, dependent on *internal cognisance* of how external factors affect one's behaviour, and the *actual ability* of control they have been afforded by these external factors; the two commonly differ. [57] The link

between actual ability and internal cognisance is self-efficacy. For an individual already familiar with infection control theory and technique, self-efficacy manifests as the confidence to actually practise what they have learnt when it is required. Alternatively, interventions seeking to increase self-efficacy of HCWs who find themselves constrained by time restrictions or the overbearing opinions of senior staff may involve improving HCW assertiveness, knowledge about hospital policy regarding patient safety, and practise in escalating concerns with other staff. [57] Training could involve testing a student's capacity to remind a HCW to decontaminate their hands after observing them failing to do so while on the wards. [57]

Summary

Why is it that HCWs fail to clean their hands? Using the TPB framework, we explored the internal behavioural factors underlying noncompliance. HCWs' beliefs about hand hygiene are informed by elements both at work and in the community. These perceptions define attitude, subjective norms and perceived behavioural control, which predict intention to clean one's hands. With this understanding, it is imperative that interventions addressing compliance do not ignore these modifiable influences on HCWs. Table 1 is a summary of interventions suggested in this article. Addressing the behavioural psychology of hand hygiene might just be the final nail in the coffin for hand-transmitted HAIs.

Conflict of Interest

None declared.

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Vocal cord dysfunction: A co-existent or alternative diagnosis in refractory asthma?

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I am a fresh graduate who is currently undergoing my internship year in Singapore. I have an interest in critical care medicine and hope to specialise in that area in the future.

Asthma is a common condition. Numerous studies have consistently demonstrated that refractory asthma, while constituting under 10% of all asthma patients, consumes a disproportionate amount of healthcare costs. It is therefore imperative for clinicians to be aware of common mimics of asthma that can present with similar symptoms leading to inaccurate assessment of asthma. One such mimic is vocal cord dysfunction (VCD), which is the intermittent, abnormal adduction of the vocal cords during respiration. VCD can exist independently, but it frequently co-exists with asthma and consequently has been frequently misdiagnosed as asthma. The gold standard for diagnosing VCD is through direct visualisation via laryngoscopy, but there has been a move towards developing alternative non-invasive means of diagnosing VCD in the acute setting. This article reviews the literature surrounding VCD, including management options, both in the acute and long-term setting.

Introduction

Asthma is a common condition. In 2011-2012 the prevalence of asthma was measured at 10.2%, which approximates to about 2.3 million Australians. [1] By international standards, this is a high statistic, translating to a significant burden on the healthcare infrastructure. An estimated \$655 million was spent on asthma in the 2008-09 financial year, accounting for 0.9% of the total allocated healthcare expenditure.

The aim of asthma management is to achieve good long-term control. However, evaluation of asthma control relies heavily on symptom assessment. [2] The National Asthma Council of Australia utilises the Asthma Score to gauge a patient's asthma control, based on frequency of asthma symptoms, nocturnal symptoms, effect on activities of daily living, as well as use of reliever medication. [3] However, it is challenging to distinguish between poorly controlled or refractory asthma versus an alternative diagnosis with a similar presentation. As such, this reliance on symptom assessment as a measure of asthma control has its shortcomings.

Numerous studies conducted across several countries have consistently demonstrated that refractory asthma, while constituting under 10% of all asthma patients, consumes a disproportionate amount of healthcare costs. [4,5] This often occurs in the setting of treatment failure and escalation of drug therapy, as well as recurrent or prolonged hospital admissions. [6] Current management guidelines advocate for clinicians to consider issues surrounding compliance, technique, as well as to reconsider the possibility of an alternative diagnosis in the context of treatment failure. It is therefore imperative for clinicians to be aware of common mimics of asthma or co-morbidities that can present with similar symptoms leading to inaccurate assessment of asthma control. One such mimic is vocal cord dysfunction (VCD).

Vocal cord dysfunction

VCD is the intermittent, abnormal adduction of the vocal cords during respiration. [7,8] It can affect both inspiratory and expiratory phases, resulting in variable upper airway obstruction at the level of the larynx. [6] VCD has been described throughout the medical literature by several terms, including Munchausen's stridor [9], factitious asthma, [10] and paradoxical vocal cord dysfunction. [11]

Dunglison first described it in 1842, referring to it as 'hysterical croup' at that time. [12] Subsequent authors documented similar descriptions



of this presentation under various names in the medical literature, but it was Mackenzie who first visualised the paradoxical closure of the vocal folds with inspiration by laryngoscopic evaluation in 1869. [13] Interest in VCD resurfaced in 1974, when Patterson et al. demonstrated modern laryngoscopic evidence of this pathology. [9] However, it was only from 1983, following a case series by Christopher et al. [14], that VCD was formally described as a syndrome, prompting a surge in interest until today.

Epidemiology

There are no large population-based studies examining the prevalence of VCD. The lack of specific diagnostic criteria for VCD further confounds evaluation of its epidemiology, leading to a range of prevalence estimates between 2.5 and 22% derived from small studies. [15] Nonetheless, it has been reported to be more prevalent among females, and is common in persons between 20-40 years of age. [16]

VCD can exist independently, but it frequently co-exists with asthma. In the first large case series involving 95 patients, Newman et al. reported 56% of patients had co-existing asthma. [8] Similarly, Yelken et al. found that VCD was present in 19% of 94 asthmatic patients, compared to 5% in 40 control subjects. [17] Parsons et al. concluded from their study of 59 patients that VCD occurs across a spectrum of asthma severity and is also prevalent in mild-to-moderate asthmatics. [18]

Correspondingly, the literature is replete with reports of VCD misdiagnosed as asthma. In a review by Morris et al. up to 380 of 1161 (32.7%) patients with VCD were initially misdiagnosed and in fact that many patients only had VCD without underlying asthma. [16] Similarly, Newman et al. concluded that VCD was the reason for treatment failure in 30% of cases in their prospective evaluation of 167 patients with refractory asthma. Among these cases, one third exclusively suffered from VCD, while the rest had co-existing asthma. [8]

Diagnosing VCD

While the gold standard for diagnosing VCD is through direct visualisation via laryngoscopy [19], this is often not frequently utilised due to practical reasons. There has been a move towards developing alternative non-invasive means of diagnosing VCD in the acute setting. Diagnostic approaches such as methacholine provocation [20] and video stroboscopy [21] have not proven useful in providing conclusive evidence to aid a diagnosis.

There is limited utility in using pulmonary function tests to diagnose VCD in the acute setting, this difficulty also being due to VCD's intermittent symptoms. VCD may reduce both the forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) with no change in the forced expiratory ratio ($FER = FEV_1 / FVC$), suggesting that such a pattern in a patient undergoing evaluation for asthma should raise the possibility of VCD. Yet, a reduction in FER as consistent with an obstructive pattern such as asthma also does not rule out concomitant VCD. [8,16,22]. A characteristic truncation of the inspiratory limb of the flow volume loop has also been described in symptomatic inspiratory VCD, with similar changes to the expiratory loops in expiratory VCD. However, a review by Morris et al. found such FVL changes to be present in only 28.1% of all VCD patients. [16]

Traister et al. developed the Pittsburgh Vocal Cord Dysfunction index as a clinical tool to aid clinicians in distinguishing VCD from asthma clinically. [23] Based on the largest to-date retrospective study comparing 89 patients with VCD and 59 patients with asthma, the authors identified clinical features such as dysphonia, throat tightness and the absence of wheezing as key distinguishing symptoms of VCD. The Pittsburgh VCD index had good sensitivity (83%) and specificity (95%), and accurately corresponded with 77.8% of laryngoscopy-proven VCD. [23]

However, Traister et al. also cautioned against the use of the scoring index in patients with both VCD and asthma. Numerous studies have concluded that differentiating one condition from the other based on symptomatology can be challenging if both conditions co-exist. [14] For example, Parsons et al. found that classic VCD features like hoarseness and stridor occurred infrequently in patients with both conditions and did not necessarily distinguish between asthmatics with and without VCD. [18]

Clinicians can also utilise several clinical signs and simple bedside tests to aid diagnosis. Localisation of airflow obstruction to the laryngeal area via auscultation is an important clinical discriminatory feature in patients with VCD. In addition to that, the disappearance or reduction of wheeze with expiration against positive pressure (via a straw) when auscultating over the larynx would suggest an element of VCD.

The introduction of high resolution 320-slice CT has permitted visualisation of the moving anatomical structures. [24] Holmes et al. explored the possibility of utilising this to provide comprehensive and accurate images of vocal cord movement during respiration. In this study, dynamic 320-slice volume CT accurately identified VCD in 4 of 9 patients diagnosed with asthma. [24] Colour Doppler ultrasound of the vocal cords has also been suggested as a potential means of diagnosing symptomatic VCD, with accuracy approximating that of laryngoscopy, according to one report. [25]

Management of VCD

Management of VCD first requires establishing the correct diagnosis. While this may be difficult in the acute setting, it is imperative as continuing to treat for asthma will not yield any benefit.

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Reassurance of the patient has been widely reported in numerous case reports as effective in terminating VCD in the acute setting. [10,26,27,28,29] Adopting breathing patterns such as panting, [30,31] diaphragmatic breathing or breathing against positive-pressure (through a straw, pursed-lip breathing) have also been described as effective measures to abort VCD symptoms acutely. Similarly, administering positive pressure ventilation via CPAP has been demonstrated in several case reports to resolve an acute attack. [32]

Benzodiazepines have been noted to be very effective in terminating VCD episodes, mainly for their anxiolytic and sedative effect. [16] Heliox, a mixture of oxygen and helium, has also been used to both treat and differentiate VCD from other causes of airway obstruction, with a rapid and effective response [33], however larger studies are lacking.

The long-term management of VCD revolves mainly around a multidisciplinary approach. Speech therapy has been identified as a mainstay treatment for VCD, with emphasis on vocal cord relaxation and breathing techniques. [34] Psychological interventions, such as psychotherapy, behavioural therapy as well as the use of anxiolytics and antidepressants have also been demonstrated in a systematic review to be useful adjuncts to speech therapy. [35]

There is a paucity of high quality randomised control trials studying therapeutic options for VCD. Botulinum toxin has been used to relieve symptoms of VCD in several cases, although its use is at present largely experimental due to the lack of research. Its neuromuscular effect of inhibiting acetylcholine release relaxes laryngeal muscles which lasts up to 14 weeks, facilitating inspiratory and expiratory airflow. [36] Baxter et al. evaluated the benefits of botulinum toxin in a small sample size of 11 patients with treatment resistant asthma and abnormal vocal cord movement. Asthma control test scores (a five-question self-administered tool), CT visualisation of vocal cord narrowing, as well as spirometry were used to evaluate response following botulinum toxin treatment. The study concluded that local treatment with botulinum toxin could be effective in these cases, although a placebo effect could not be ruled out. [37]

Conclusion

The novel utilisation of existing imaging techniques has facilitated the diagnosis of VCD, a condition that has been described since the 19th century, yet it continues to remain a diagnostic challenge because it demands certain level of clinical suspicion prior to further workup. There is also a lack of awareness of its existence and its presentation consequently has often been attributed to asthma. This is further complicated by its common coexistence with asthma, which can lead to unnecessary medication use without beneficial impact and increased health care utilisation.

Conflict of interest

None declared.

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The gender imbalance in ADHD

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The gender imbalance in ADHD

Attention-deficit/hyperactivity disorder (ADHD) is a highly prevalent neuropsychiatric condition placing a considerable burden of disease on our population. ADHD primarily manifests in childhood with symptoms of inattention, hyperactivity and/or impulsivity that affect normal function. [1] Though ADHD affects both children and adults, current literature has focused greatly on the disorder in children and this paper will focus mainly on the paediatric population. Australian statistics reported ADHD as the leading mental and behavioural condition amongst children 0-14 years of age, accounting for 12% of children with a disability in 2004. [2] Furthermore, the diagnosis of ADHD in paediatric consultations has increased in frequency to almost 18% of the referred population. [3] Unfortunately, the prevalence of ADHD has been difficult to assess due to its heterogeneous nature and dependence on diagnostic criteria and classification. [4] Despite these obstacles, the reported demographic of ADHD has illustrated a skewed gender distribution towards males worldwide, creating a scope for exploring the gender differences in ADHD. [5-7] Current research has focused on theories supporting changing diagnostic criteria, phenotypic differences and biological differences to explain this gender difference in the prevalence of ADHD. However, to better understand this gender distribution, it is important to understand the terminology utilised in ADHD and how this has influenced current prevalence estimates for the disorder.

Definition of ADHD

The terminology and criteria surrounding ADHD have undergone significant revision over time. On the whole, it should be emphasised that normal childhood development displays active, impulsive and inattentive behavior and diagnosing ADHD should be based on a comprehensive subjective and objective assessment of the individual. [1] The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM) provides specific criteria for diagnosing ADHD, but is also a prime example of the changing definition of the disorder. [1] ADHD was initially defined as a hyperkinetic reaction of childhood in the DSM-II, followed by Attention Deficit Disorder, with or without hyperactivity, in DSM-III, and finally ADHD with subtypes presented in DSM-IV. [8] The DSM-V now defines ADHD as pattern of inattention and/or hyperactivity-impulsivity that is persistent, interferes with development, has symptoms presenting in two or more settings, and directly impacts on the individual's functional capabilities. [9] The core symptoms of inattention and hyperactivity-impulsivity each contain their own set of symptoms, of which six or more must be present in children and five or more in adults for at least 6 months prior to assessment. [9] The DSM-V has also reframed subtypes of ADHD from the DSM-IV to presentations including combined presentation, predominantly inattentive presentation and predominantly hyperactivity-impulsivity presentation. This evolving terminology has been implicated in many studies attempting to explain the differing prevalence of ADHD across the world, which, in turn, influences the gender distribution of ADHD.

Prevalence of ADHD

ADHD is a heterogeneous disorder with symptoms requiring both temporal and spatial conditions and the lack of definite diagnostic tools has prevented an accurate representation of the disorder worldwide. [4,8,10] Firstly, there are variations in methodology, including the diagnostic criteria used and evaluation of clinical impairment. [4] For



example, studies may illustrate increased rates of childhood ADHD classified using the DSM-IV criteria but decreased rates in those who undergo further assessment, suggesting diagnostic inaccuracy. [10] Furthermore, a recent community-based study in America illustrated increasing prevalence estimates with the new DSM-V criteria for age of onset and symptom count, but decreasing prevalence with the new criteria requiring a degree of impairment due to the disorder, based on changing case definitions of ADHD. [8] Overall, there are strengths to having accepted diagnostic criteria in the DSM, however the lack of tools to identify and quantify these symptoms continues to be an obstacle in current prevalence estimates for ADHD.

In addition, the population sample (e.g. community or clinic) contributes greatly to varying prevalence estimates. [4] For example, an Australian study based on participants identified in a parental-reported survey illustrated an ADHD prevalence of 13.6% with a male: female prevalence ratio of 2:1. [6] Conversely, an Australian clinical study showed a greater gender difference with a male to female ratio of 4:1. [3] This illustrates a well-recognised pattern in the prevalence of ADHD where male to female ratios are higher in referred populations than in community-based samples. [4,7,11] The main explanation for this evident gender distribution between the population samples has widely been accepted as referral bias, whereby a myriad of factors has resulted in a greater number of males reaching clinics for diagnosis and management of ADHD. [11] There have been many factors found contributing to this referral bias including phenotypic differences, recognition of comorbidities and symptom reporting amongst the ADHD patient population. [11] Overall, the skewed gender distribution in ADHD prevalence is influenced by both methodology and population variables and these need to be carefully considered when analysing the role of gender in ADHD.

Phenotypic differences in ADHD

ADHD presents with a myriad of manifestations that share the underlying characteristics of inattention and/or hyperactivity. In general, the main differences in symptom recognition for ADHD differs with males being more likely to be recognised for externalising symptoms in contrast to females exhibiting internalising features. [5,7,12] These symptoms can be further described as males more likely to present with disruptive behaviours that correspond to the hyperactive-impulsive core symptoms whereas females are more likely to present with symptoms correlating to inattention. [6,7,10,12] Multiple studies have also shown

that females are more likely to exhibit physiological anxiety, whereas males were reported for rule breaking and risk taking actions. [6,12] Females were also more likely to present with somatic complaints, which have been considered a marker for anxiety proneness across the literature. [7,12]

Furthermore, the recent inclusion of ADHD subtypes has added to the gender differences in ADHD, where females are found more likely to be diagnosed with predominantly inattentive ADHD whereas males are more commonly diagnosed with predominantly hyperactivity-impulsivity or combined presentations. [12,13] This, in turn, has consequences on the aforementioned referral bias, where females who are identified to have symptoms of ADHD were not considered impaired if exhibiting inattentive ADHD, but considered severely impaired when exhibiting hyperactive-impulsive ADHD. [11,13] Another implication of these subtypes is the tendency for hyperactive and/or impulsive behaviour to lessen over time whereas inattentive behaviour tends to persist. [1] This, in turn, may lead to more males being recognised for their ADHD in childhood due to an increased tendency to express hyperactive/impulsive behaviour and for female patients to be under-recognised. [13] Phenotypic differences in ADHD play an important role in ascertaining the gender distribution of this disorder as these differences may result in referral bias and therefore account for the greater number of males recognised with the disorder. [11,13]

Comorbidities in ADHD

Comorbidity in childhood psychiatry is an expected phenomenon, with ADHD commonly presenting with common concurrent neuropsychiatric conditions. [14] For example, disruptive behavioural disorders such as oppositional defiant disorder have a high rate of comorbidity with ADHD, sharing particular symptoms with the hyperactive or impulsive subtype. [14] Similarly, anxiety disorders are also commonly diagnosed in patients with ADHD, usually with a more severe and distinctly inattentive clinical presentation. [15] Furthermore, these childhood psychiatric disorders appear to illustrate a similar gender distribution to that of ADHD, with disorders such as autism spectrum disorder being widely accepted to have a male predominance in childhood. [16] However, reports of comorbidity in ADHD is subject to the same limitations of referral bias, phenotypic differences and diagnostic criteria that influence the prevalence and gender distribution across childhood psychiatry. [14]

Furthermore, both males and females have been found more likely to have comorbid ADHD, in comparison to a solitary diagnosis of ADHD [17] Some studies have shown parents and teachers to report more difficulties with oppositional behaviours, social difficulties, depression and anxiety in females, compared to their male counterparts. [12] However others have illustrated an equal increase in presentation of comorbid conditions in the hyperactivity-impulsivity subtypes, with the gender difference being higher levels of comorbidity for females in the inattentive subtype through comorbid social and generalised anxiety disorders. [17] Another study found the only statistically significant gender difference to be a higher rate of substance use disorders in females with ADHD, particularly in early adolescence. [13] Overall, comorbidity in ADHD is an important consideration in studying the prevalence of the disease and how the gender distribution of these disorders can influence the gender distribution of ADHD.

Symptom reporting in ADHD

Firstly, many studies have commented on symptoms reported by patients, parents, teachers and clinicians – all of which provide different criteria for diagnosis of ADHD. Studies have shown self-reported symptoms to be highest in the clinical setting, whereas community-based research focuses heavily on parent- and teacher-reported symptoms. [12] A review of variations in ADHD prevalence mentioned that multiple studies have shown different rates of symptom reporting between parent and teacher. [4] Teachers' contributions are substantial as they can provide daily observations of patients in

comparison to unaffected individuals of the same age, environment and developmental level. [4] Parents are also valuable as they provide a change in an individual's behaviour over time. However, both groups lend themselves to symptom recognition biased towards hyperactivity and impulsivity, as these tend to be more disruptive in both the school and home environment. This results in under-recognition of internalising symptoms such as depression and inattention, which, in turn, influence the rates of symptom reporting for ADHD. [4,12]

Furthermore, the culture surrounding ADHD has resulted in it being considered a male disorder. [5,10] This has multiple implications, from a greater tendency to recognise symptoms in the community to specialist referral for ADHD symptoms, with the social and cultural constructs of ADHD making males more likely to be subject to symptom reporting. [7,10] The lower prevalence rates have also been attributed to the higher likelihood of referral for disruptive behaviour, more commonly seen in the hyperactivity-impulsivity presentation or combined presentation of ADHD [11]. This, in itself, creates a skewed gender distribution as these have been illustrated at higher rates in the male population. [5] On average, there are more similarities than differences in the symptomatology of ADHD across genders, and symptoms are not sex-specific, but rather show trends as discussed above. [5,13] However, it is important to be aware of the gender differences when applied to ADHD subtypes, comorbid psychological conditions and the sources of symptom reporting for accurate diagnosis and management of ADHD in our population.

Biological Differences in ADHD

Biological factors have also been shown to influence gender differences in ADHD prevalence in our population. However, the majority of research conducted in this field has been underpowered due to the disproportionate number of males diagnosed with the disease, and the lack of drive to characterise any prospective sex differences. [18] A recent review discussed the evidence for neurogenetic and endocrine mechanisms, where differences in chromosomal composition, sex-linked genes and early exposure to hormones can interact to affect the manifestation of ADHD between sexes. [19] For example, there is an inherent sex difference in the male-limited expression of the Y chromosome and the presence of only one X chromosome, which leads to the presence of different genes and mutations that may influence neurodevelopment and susceptibility to ADHD between genders. [19]

Furthermore, there is increasing research into the anatomy and physiology of the neurological aspects of ADHD. This has illustrated a complex network of brain regions that are structurally modified to produce a developmental deviation in response to immature cortical under-arousal. [18] This has also produced gender differences whereby electroencephalography (EEG) studies have shown different patterns between males and females, and further differentiation between ADHD subtypes. [20] Overall, the current literature has emphasised a need for more focused research on the biological differences in ADHD to better characterise the profile of ADHD in males and females.

Management of ADHD

The implications of gender differences on the diagnosis and identification of ADHD have been discussed, however it is important to also consider the impact of gender on the management of ADHD. Pharmacological management in the form of stimulant medication has recently been gaining traction in current treatment practices for ADHD. [3,21] In general, current trends have shown that males with ADHD are more likely to receive pharmacotherapy and psychotherapy than females. [13] For example, in Western Australia, the prescription rates for stimulant medication were greater in males than females. [22] NSW Public Health illustrated a similar pattern, with males four times more likely to be on stimulant medication than females, though there has been an increase in the prescription patterns for females over the last two decades. [23] These statistics elucidate gender differences in practitioner trends and management of ADHD, however further investigation would be required to explain these trends in correlation

to the disease recognition and prevalence as discussed earlier. In addition, it is also important to consider the possibility of gender differences in the treatment response for ADHD, though a recent population-based study has shown the response was favourable and did not differ between genders. [24]

In addition to pharmacological management, there is an increased role of behavioural intervention in the management of ADHD. Behavioural therapy represents a collection of specific interventions that modify the physical and social environment in order to change behaviour. [21] These interventions can be delivered through parental, classroom or peer interventions that reward desired behavioural traits and discourage undesirable behaviours through techniques such as planned ignoring, appropriate consequences and/or punishment. [21] When considering individual behavioural intervention in ADHD management, females are said to benefit from management of comorbid conditions such as mood and/or anxiety disorders that may exacerbate the expression of ADHD in combination with pharmacotherapy. [25] Mixed-gender treatment is another option for behavioural intervention in ADHD, which involves group-based behavioural interventions with both male and female patients. However, studies have shown gender differences to influence this management strategy as the mixed-gender setting may suppress treatment effect in females and fail to address gender-specific social impairments. [26] A recent American study investigated the effects of single- versus mixed-gender treatment for adolescent females and found females were more likely to benefit from single-gender treatment with more assertiveness, self-management and compliance. [26] Conversely, males exhibited lower levels of physical and relational aggression and better self-management and compliance in the mixed-gender setting. [26] Overall, behavioural intervention is important in the management of ADHD and needs to account for gender differences in disease presentation and response to treatment.

Future directions in ADHD

ADHD is rapidly gaining awareness for its burden of disease in our paediatric population. However, current literature has lacked focus in characterising important epidemiological trends in ADHD, such as the distribution between genders. Firstly, most of the discussion above has been based on studies using the DSM-IV criteria for diagnosis and therefore further studies based on the DSM-V criteria may again alter the gender prevalence of the disorder. Secondly, study design needs to account for population sample bias, especially between community- and clinic-based samples, in order to better estimate the disease and gender prevalence across the world. Studies also need to be designed

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with the aim of defining the phenotypic differences and the direct impact of these on symptom reporting in order to tailor future practice and better recognise ADHD throughout the population. The same should apply to biological differences and response to management, both pharmacological and behavioural as the main examples, for more effective clinical practice. It should also be noted this discussion focused mainly on paediatric ADHD, however current literature has seen rapid growth in research into adults with ADHD, though it is limited with regards to the gender distribution in these populations. Similar to the evidence discussed above, it is reasonable to expect the gender ratios in ADHD prevalence to be similarly affected by referral or identification bias, poorly defined diagnostic criteria and biological differences. [27] On the whole, the consensus across current literature is a need for further investigation that can better define the prevalence of ADHD in our population and the influence, if any, of gender.

Conclusion

ADHD is an increasing burden of psychiatric disease for our paediatric population with a reported greater prevalence amongst male patients. The skewed gender distribution of the disorder has been widely varied due to differing diagnostic criteria, terminology and research methodology. The differences found illustrated variation in disease presentation and psychological comorbidities, as well as biological differences that may account for the variation in disease presentation between genders. Furthermore, there were differences in reporting of ADHD symptomatology between patient, parent, teacher and clinician as well as differing trends in management that may influence the recognition and treatment of ADHD across our population. Overall, these differences warrant further research to better understand ADHD and characterise the disease profiles between males and females for increased accuracy in identification, diagnosis and treatment in our population.

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Conflicts of Interest

None declared.

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Clinical implications of the sex and gender differences associated with substance use disorders

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Arunima was a final year medical student at the Australian National University (ANU) at the time of writing this article. She previously completed a Bachelor of Science majoring in Pharmacology at the University of Melbourne. This article stemmed from a reflective piece on perspectives of Gender in Medicine as a part of the Social Foundations of Medicine framework at the ANU Medical School.

Substance use disorders are exceedingly complex management issues which result in significant medical and social consequences. Epidemiological studies in the United States and Australia show that more men than women are affected by substance use disorders. However, there is evidence to suggest that women have distinctly different and potentially more hazardous patterns of substance use. These include: a greater tendency to escalate usage, relatively higher rates of relapse, and the telescoping phenomenon (which results in a more rapid progression from the initiation of substance use to drug dependence and adverse medical consequences). Proposed mechanisms for the variable impact of substance use disorders on men and women include biological and gender-based theories which incorporate environmental, psychological and social factors. Studies attribute the biological differences to direct and indirect oestrogen-mediated mechanisms, and the influence of dopamine on structures in the brain including the nucleus accumbens and striatal pathways. Psychosocial variables include psychiatric co-morbidities, family responsibilities, financial issues and perceptions of stigma. The differences in the progression and outcomes of substance use disorders between men and women pose the question as to whether their management can be enhanced by a gender-specific approach. This article outlines the various treatment facilities available in Australia and explores the types of facilities that women tend to use. Gender-specific programs and/or facilities have been shown to be most useful when they support sub-populations of women such as pregnant mothers, mothers with dependent children, and victims of domestic or sexual violence.



Statistical Manual of Mental Disorders 5 (DSM-5) combines substance abuse and dependence associated with both licit and illicit drugs, which were previously distinguished in DSM-4. [13] Where possible, we refer to substance use disorders based on DSM-5 criteria. However, DSM-4 terminology is retained in order to maintain consistency with previous epidemiologic studies and data.

Differences in epidemiologic data, psychological factors, and clinical management may exist between the various types of substances; however, this article will focus on general principles in order to better understand sex and gender differences associated with substance use disorders and management options.

Licit drug use disorders refer to the legal use of legal drugs. Tobacco and alcohol are the most frequently used drugs – 15% of Australians over the age of 14 were daily smokers in 2010 while 24% were ex-smokers. [1] In 2012, approximately 78% of all Australians aged 14 and over drank alcohol during the year, with 18% drinking at harmful levels. [9]

Illicit substance use disorders, on the other hand, refer to the illegal use of legal drugs or use of illegal drugs. Although relatively uncommon compared to licit drugs, approximately 42% of Australians aged 14 and over reported using illicit drugs in their lifetime, with 15% reporting use in the last 12 months. [9] Cannabis, followed by ecstasy and hallucinogens were the most common illicit drugs used.

There are consistent reports that suggest a higher prevalence of substance abuse in men relative to women. [1-7] This is in keeping with data from the Australian Bureau of Statistics pertaining to Gender Indicators, which showed that men reported higher rates of substance use disorders in the year prior to data collection (7% males relative to 3% females) and throughout their lifetime (35% males relative to 14% females). [7] This is consistent with studies conducted in the United States (US) where, for example, a large survey of over 40,000 adults stated that men are twice as likely (13.8%) than women (7.1%) to address DSM-4 criteria for any drug use disorder.[3]

However, women have distinctly different patterns of drug use, which may be explained by a combination of sex and gender differences. [2,12] For instance, studies show that women tend to escalate drug use (relevant to alcohol, cannabis, opioids and cocaine) relative to men, which contributes to notion of the ‘telescoping phenomenon’.

Introduction

Both licit and illicit drug use contribute to a significant financial and disease burden in Australia. [1] Currently, epidemiological data suggests that more men are diagnosed with substance use disorders relative to women. [1-7] However, there are sex and gender differences which distinguish patterns of addiction and behavior in both groups. These sex differences have a biological basis, with associations between oestradiol-related central pathways and the propagation of drug seeking behaviours in women relative to men. [2,6,8]

The difference in the prevalence and impact of substance use disorders between genders incorporates environmental, psychological and social factors. Currently, fewer women access drug treatment programs relative to men. [9] This may be representative of the fact that fewer women suffer from substance use disorders, however it may also reflect hindrances towards seeking or accessing treatment. Such barriers towards treatment include increased perceptions of stigma, dependent family members, and financial circumstances. [10-12]

Therefore, although more men are diagnosed with substance use disorders, a different approach towards prevention and treatment may be required for women. A review of the current literature is necessary to question whether an argument can be made to support gender-specific programs to address substance use disorders.

Definitions, epidemiology and gender differences

The term ‘substance use disorder’ as defined in the Diagnostic and

[2,6,12] The term suggests that the development of behavioural, psychological and medical consequences of a substance use disorder occur at a faster rate in women relative to men. [2,12] Notably, despite the use of relatively smaller quantities of drugs within a shorter timeframe, women show greater rates of adverse social and medical consequences. [3] Furthermore, Becker and Hu's review [2] suggests that once drug addiction has been established, women find it more difficult to quit and are more prone to relapse following periods of abstinence in comparison with men.

Therefore, despite the fact that quantitatively more men may suffer from addiction, the differences in the pattern of drug seeking behaviour, escalation to use disorders, and treatment retention need to be addressed.

Sex differences

Sex differences relevant to drugs of addiction have been evidenced in both animal and human models. [2] Animal studies performed on rodents suggest that females are more likely to self-administer drugs of addiction (in this case cocaine) and have oestradiol-associated mechanisms to further propagate drug seeking mechanisms which are not present in male rodents. [2,6]

Oestrogen-mediated sex differences are evident in most phases of drug abuse including acquisition, maintenance, escalation and relapse. [2,8] Proposed mechanisms for this effect include direct interactions with the striatum and nucleus accumbens to facilitate dopamine release, and indirect interactions via sensitisation of receptors and changes in neuronal excitability. [6,8,14] The alterations in dopamine release act to regulate neurochemical responses and behaviours in favour of addiction, particularly to psychomotor stimulant drugs. [6,14]

Another contributing factor to the sex differences in drug addiction is the effect of the menstrual cycle on motivation behaviours. The impact of the menstrual cycle seems to be variable depending upon the timing of the cycle, hormone concentrations, and type of substance abused. For instance, increased euphoria, desire, and energy levels are enhanced when using cocaine in the follicular phase relative to the luteal phase. [2] In support of the notion that oestrogen plays a role in the perceived effects of drugs of addiction, the addition of oestradiol during the follicular phase resulted in a self-reported increase in the euphoric effects of dexamphetamine. [2]

Additionally, a review of 13 studies that investigated the impact of the menstrual cycle on smoking cessation suggested that women experience greater tobacco cravings and negative affect responses to tobacco withdrawal during the late luteal phase, where oestrogen and progesterone levels are diminishing. [2] The proposed mechanism for this is that the relatively higher oestrogen levels in the follicular phase may 'alleviate some of the negative consequences' associated with quitting smoking. Becker and Hu [2] support this theory by identifying a study that confirms the relationship between oestradiol, positive affect and decreased anxiety.

The variations in drug use and withdrawal symptoms during the menstrual cycle, such as increased euphoria when using cocaine during the follicular phase versus enhanced negative affect responses to tobacco withdrawal during the luteal phase, suggest that fluctuating oestrogen levels can have an impact on subjective experiences of substance use disorders.

It is difficult to truly isolate biological differences from psychosocial issues that may impact on the development and management of substance use disorders. However, there is evidence to support the significance of biological variations on the subjective experiences and outcomes associated with substance use disorders. These include the relationship between oestradiol and addiction behavior in animal studies, variations in drug-related experiences during the menstrual cycle, and the notion (detailed above) that women have a greater tendency to escalate drug use and develop adverse medical/

psychological effects as a consequence of substance use disorders. The question remains as to whether the telescoping phenomenon in women requires a different management approach – are there any benefits of targeting women through specific programs or do mixed-gendered programs and facilities suffice?

Psychosocial differences

In addition to the identified biological differences in substance use disorders, psychosocial factors may contribute to variations in addiction behaviours, treatment initiation and outcomes. Such factors include, but are not limited to, psychiatric co-morbidities, dependent family members, financial issues and perceptions of stigma.

Studies suggest that women with substance abuse disorders are more likely to have a prior diagnosis of a psychiatric disorder relative to men, with more women meeting criteria for anxiety, depression, and eating disorders. [3] Potential contributing factors to this difference in mental health outcomes include higher rates of experienced trauma such as sexual abuse and/or intimate partner violence, disrupted family environments, and a perception of over-responsibility (such as caring for a child or other family members) in women relative to men. [3,10,11,15] The correlation between psychiatric disorders with substance use disorders urges the need for more holistic treatment. Specialised services that incorporate mental health into the management of substance use disorders have shown to yield better outcomes with respect to treatment retention and continuity of care. [16]

In addition to psychiatric co-morbidities, previous studies document a greater perception of stigma amongst female substance abusers, whereby women experienced higher levels of guilt, embarrassment and shame relative to males. [11,15,17,18] This has an impact on the willingness to seek and/or continue treatment not only for substance use disorders but other necessary community services. The Network of Alcohol and Other Drug Agencies (NADA) report suggests that women identified having difficulty accessing services such as pre-natal classes and housing support due to perceived stigma, discrimination and fear of judgment from child protection services. [11]

Social factors that hinder management of substance use disorders in women relative to men include: lower education levels and financial income, housing issues, interaction with child protection services, and dependent children and/or other dependent family members. [10-12] Green's research [10] and NADA's report [11] suggest that women experience relatively greater difficulty in finding time to attend regular treatment sessions due to family responsibilities and transport issues. The social factors mentioned above, in conjunction with the perception of stigma, act as significant barriers for women to access treatment. These need to be addressed in order to successfully promote women to seek initial treatment while providing necessary support to facilitate long-term management.

Current use of treatment facilities

Briefly, the types of treatment facilities in Australia as outlined by the AIHW's report include [9]:

- Assessment only, whereby agencies identify the severity of the issue and refer accordingly
- Information and education only
- Support and case management only
- Counseling for individuals and groups through methods such as cognitive behavior therapy
- Withdrawal management (home, in-patient, or out-patient)
- Rehabilitation (residential treatment services, therapeutic communities or community-based rehabilitation)
- Other holistic approaches, which include relapse prevention, living skills classes, safer using, etc.
- Other health services include GP visits, hospital treatment and homelessness services.

In Australia, fewer women (32%) received treatment through alcohol and other drug treatment services relative to men (68%) in 2012-2013, which is consistent with studies conducted in the US where extensive research regarding the impact of gender on substance abuse is conducted. [9] It is unclear whether the reduced proportion of women seeking treatment is solely reflective of the relatively smaller number of women with addiction issues, or also inclusive of the financial and psychosocial factors that can prevent women from seeking treatment. [9]

Studies based in the US allow for the identification of gender differences between the types of facilities used for managing substance abuse disorders. Women are more likely to approach mental health or primary clinics rather than addiction treatment programs or specialty clinics. [3,19] It is proposed that this may be due to the perception that the psychological distress and impairment associated in those with substance use disorders may be better addressed by directly treating the mental health issue. [19]

There is limited research regarding the impact of this preference on treatment outcomes, however Mojtabai's study [19] found that this pattern of treatment was less effective when compared to participants who sought help in specialty settings. [10] Management through facilities dedicated to substance use disorders was associated with a relatively reduced likelihood of continued substance use, with fewer participants reporting alcohol and substance use in the past month. [10,19] The study urges for better integration of substance use disorder management in the mental health system, and an efficient referral system across the 'traditionally separate systems of care'. [19]

Future directions: utility of gender-based programs?

Services that provide comprehensive support by addressing medical, psychiatric and social issues (such as employment or child protection) have been shown to improve attendance, social adjustment and relapse rates in both men and women. [12,20] Previous research suggests that gender does not seem to predict patient retention, treatment completion, or patient prognosis once an individual begins treatment. [12] This seems to contradict the need for gender-specific programs, considering that treatment appears to offer equal benefit to both men and women. However, this needs to be considered in light of the fact that there are differences in the rates of treatment access between men and women, which may be explained in part by the psychosocial factors outlined above.

There is evidence to suggest the benefit of gender-specific programs or facilities in certain contexts. These include programs that focus on female-specific topics such as sexual abuse and body image, residential facilities for women with dependent family, and tailored care for pregnant mothers. [10,21] In 2005, the Drug and Alcohol Services Information System (DASIS) report in the US suggested that 41% of substance abuse treatment facilities that accepted female clients provided additional support programs specifically for women. [22] There are gender specific programs and facilities, including those dedicated to pregnant women, in most Australian states – although they may not be as numerous as those available in the US. For instance, out of 28 Network of Alcohol and Other Drug Agencies services in New South Wales, Australia, 7 provided women-only services. [11]

Gender specific psycho-education sessions on topics specific to women have received positive feedback in a few different studies. [11,16,19] These sessions allow for the discussion of more sensitive issues such as domestic violence, sexual abuse, parenting, weight and body image in a more comfortable scenario. [10,11,21] It is crucial that these programs are flexible and avoid the use of a confrontational style. [16] The presence of dynamic and interpersonal discussion is considered beneficial, and is suggested to occur more often and in an uninterrupted fashion in women-only programs. [16] The importance of self-expression without interruption is highlighted by the fact that unaddressed issues may result in adverse psychological effects. [16] Specific interventions that have been proven to be effective include

but are not limited to: parenting skills for mothers on methadone maintenance, relapse prevention for women with post traumatic stress disorder, and relapse prevention for women with marital distress and alcohol dependence. [10,11,12]

Programs specific to women tend to offer facilities that allow for accompanying children (through child care support during clinics and day programs), and may also provide residential facilities for the client and dependent family. Such facilities have been shown to have better treatment outcomes including longer lengths of stay. [11,12,16] Furthermore, family inclusive practices may have services that aim to repair relationships with children and family members thus enhancing support systems and the quality of the home environment.

Pregnant women with substance use disorders can be at high risk of numerous medical and social issues affecting their mental and physical health, which in turn impacts upon their risk of obstetric complications and the subsequent health of their baby. Pregnant women are more likely to: be of younger age, have previously given birth, have limited social supports (including limited financial stability) and have a concomitant psychiatric diagnosis. Such populations require a multitude of coordinated services and can significantly benefit from residential services, which allow for increased social support for themselves and dependent family. [11] Programs dedicated to pregnant and perinatal women have demonstrated significantly improved patient engagement and pregnancy outcomes. [12,23,24] Specific intervention programs that have yielded beneficial results for expecting mothers include alcohol interventions for pregnant women, contingency management to increase abstinence in pregnant women, and comprehensive service models for pregnant women such as access to prenatal care. [11] The benefit of customised care was highlighted by a study which recorded higher infant birth weights (2934 grams vs. 2539 grams) and a smaller proportion of neonatal intensive care admissions (10% vs. 26%) when comparing cocaine-dependent mothers who received twice-weekly addiction counseling with those who did not. [23]

In addition to gender-specific treatment, future directions may include a transition to more gender-sensitive services. [10] Suggested strategies include: matching therapist and client gender, mixed-gender group sessions concurrently led by both male and female leaders, and gender-specific treatment information or content. [10] The results of client and therapist gender matching are unclear. Some studies suggest that clients reported a sense of greater empathy resulting in longer treatment durations and lower rates of relapse, whilst other showed no difference in outcomes. [10]

Conclusion

There are documented sex differences with respect to substance use disorders through direct and indirect oestrogen-mediated mechanisms, the dopamine influence on nucleus accumbens and striatal pathways, and variable impacts of the menstrual cycle. These occur in addition to gender differences, which incorporate psychosocial variables such as psychiatric disorders, family environment, domestic violence, and social stigma. Currently, men experience higher rates of substance abuse relative to women; however, women are more likely to escalate drug use and suffer from biological and/or psychological consequences at lower doses and shorter durations of drug use. Additionally, women are less likely to enter treatment relative to men.

Studies provide inconclusive results regarding the benefits of gender-specific programs over those that have a gender-mix. However, there may be a need to support sub-populations of women including pregnant mothers, mothers with dependent children, and victims of domestic or sexual violence. Therefore, future directions include the need to increase awareness regarding substance use disorders, facilitate treatment for women in general, provide ongoing support to relevant subgroups, and consider a more gender-sensitive approach during management of substance use disorders.

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Conflict of Interest

None declared.

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The Magic Number: The case for a 21-year-old minimum drinking age in Australia

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The United States is unique among Western countries in setting the minimum legal drinking age at 21 years. The choice of 21 was largely driven by a powerful road-safety lobby group in the 1980s; however a wealth of clinical and epidemiological evidence has subsequently emerged in its favour. A highly-publicised article in the *Medical Journal of Australia* [1] recently proposed raising the Australian minimum drinking age from 18 to 21, citing both sociological and neurodevelopment arguments. This essay reviews the three conditions that should be satisfied for such a legislative change to occur, and proposes an alternate license-based model for age regulation as a thought experiment.

Age-21 Laws in the 21st Century

When prohibition ended in the United States in 1933 with the 21st Amendment, states were given autonomy to set their own alcohol regulations. This included the minimum legal drinking age. The commonest age chosen was 21 years (in 32 states), followed by 18 years (13 states), 20 years (3 states), and 16 years (in Ohio). [2] 21 was likely favoured because, at the time, this was the age of majority in most US states – the age when an individual was legally considered an adult, the age when they could vote in state elections. [3]

Forty years later, in the midst of the Vietnam War, the issue of drinking age emerged once again into the spotlight. A public campaign argued that it was nonsensical for a man to be conscripted to the army, be sent abroad to fight and die for his country, and yet not legally be permitted to have a drink. One by one, under strong public pressure, the states lowered the drinking age to 18 years. [3] This coincided with changes in the age of majority at a federal level. The 26th Amendment of 1971 gave 18-20 year-olds the right to vote in the United States – 18 years became the age of adulthood.

However, while voting rights persisted for 18-year-olds, this lowered drinking age lasted but one generation. In 1984, the Reagan administration passed the *National Minimum Drinking Age Act*, which raised the legal drinking age to 21 again. [4] To expedite the change, the federal government threatened significant infrastructure cuts to any states that did not comply. By 1988, alcohol was banned for under-21s in all 50 states and territories across America. Even Ohio.

The strongest lobby group in support of this raised drinking age was “Mothers Against Drunk Driving” (MADD) – a not-for-profit organisation run by mothers of the victims of alcohol-fuelled driving accidents, many of whom were under the age of 21. [5] MADD claims that this legislation has saved over 25,000 lives since 1988, purely from traffic-related morbidity. [6] Subsequent evidence has confirmed that a 21-year old drinking age has benefits far beyond road safety, reducing the incidence of alcohol dependence [7], alcohol-related violence [8], suicide [9], and risky sexual behaviours amongst youth. [10] More recent neurodevelopmental evidence has bolstered the case, demonstrating that alcohol exposure impairs neuronal maturation in under-21s. [11] Consequently, the US persists in this awkward legislative balance where individuals can vote, drive and enlist in the army at 18, but cannot yet purchase a beer.

This is not unique from an international perspective in that 6 other nations have a 21-year minimum drinking age: Sri Lanka, Indonesia, Kazakhstan, Oman, Pakistan and Palau. [12] In all these cases, the



choice of 21 was driven far more by cultural and religious factors than epidemiological evidence. The closest other OECD nation is Japan, with a drinking age of 20. The vast majority of countries have chosen 18 years, in line with the standard age of legal majority. Switzerland, Belgium, Austria, Germany, and the Netherlands have all chosen an age of 16.

Advance Australia where?

Although it is clearly not the mainstream position internationally, public support is growing for a 21 year minimum drinking age in Australia. In 2010, 50.2% of respondents supported such a change, compared to 40.7% in 2004. [13] In a 2014 article in the *Medical Journal of Australia*, Toumbourou et al. elegantly assembled the case for a 21-year threshold [1]. The article gained significant media attention in May 2014, catapulting the issue of drinking age into the spotlight – not for reasons of youth enfranchisement (as in the Vietnam era), not for reasons of road safety, but with a comprehensive clinical and epidemiological argument behind it. The National Alliance for Action on Alcohol and the Australian Medical Association have added weight to this “age-21” campaign. But is this a realistic option for Australia? In the delicate balancing act between theoretical goals and practical realities, what age is the magic number? Is a single age too simple?

The burden of proof

Any case for age-21 legislation in Australia should demonstrate three key points:

- (i) That alcohol consumption at 18-21 years causes significant negative outcomes
- (ii) That age-21 regulations are effective at reducing the alcohol intake of under-21s
- (iii) That the benefit of alcohol restriction outweighs the value of preserving 18-21 year olds’ autonomy

The reason point (iii) is necessary is that points (i) and (ii) are likely true for all age groups: restricting alcohol purchase would presumably reduce alcohol consumption and therefore alcohol-related complications irrespective of age. As a society, we have made a policy decision to tolerate alcohol use despite its associated risks in the interests of public autonomy. So the real question here is whether under-21s are disproportionately affected by alcohol-related risks to the point that this autonomy should be overridden and all consumption legally forbidden. Is the 18-21 age group really so vulnerable?

Condition 1 – An age of vulnerability

There is accumulating evidence to suggest that 18-21 year olds are a population at extreme risk from alcohol-related complications based on neurodevelopmental, road-safety, and behavioural data.

1. Neurodevelopmental

Cross-sectional studies have shown that alcohol consumption during adolescence is associated with short- and long-term cognitive impairment, including deficits in information processing, memory, attention and executive function. [11,14] This is especially true for binge drinking behaviours. [15] Structurally, there appears to be impaired white matter development in the prefrontal cortex and fronto-striatal circuitry, which has been demonstrated with CT [16], fMRI [17] and post-mortem data. [18] However, some critics have argued that these neurobiological variations may be pre-existing features that predispose individuals to alcohol experimentation, rather than the consequence of alcohol abuse. For example, in a recent review article Clark et al. [19] suggest that studies have not sufficiently controlled for confounding psychological variables, such as attention deficits and disruptive behaviours, which are known to be associated with early alcohol experimentation. To clarify the causal links, further longitudinal data is required assessing the baseline neurobiological status of adolescents before their first alcohol exposure.

2. Road safety

A 2001 meta-analysis of 9 population studies found that raising the minimum legal drinking age from 18 to 21 caused a 12% reduction in overall road-related mortality. [20] This aligns with the data collected by MADD and the National Highway Safety Administration in the United States [6]. However, the question arises whether these improvements in road safety are age-specific. Would raising the drinking age to 25 also cause a 10% drop in accidents among 21-24 year-olds? The argument is that 18-21 year-old drivers are the least experienced, the least responsible, and therefore the most vulnerable to alcohol. However, there is a lack of rigorous data to demonstrate age-specificity. The legal alcohol limits for driving in Australia are somewhat age-dependent, with L- and P- drivers having a zero blood-alcohol tolerance, compared to 0.05% for full-licensees. Does a differential blood alcohol threshold provide adequate protection to account for the clear difference in risk profile between adolescents and older drivers? [21]

3. Risk behaviours

Beyond road-related accidents, there is strong evidence to suggest a broader correlation between alcohol use and risky behaviours. A survey of Australian 17-19 year olds on "Schoolies" showed that 64% had consumed more than 10 drinks on a single occasion, and 18% displayed risky sexual behaviours. [22] A survey of almost 9000 American adolescents 12-21 showed a striking correlation between alcohol excess and physical violence [23]; while Miller et al. argue that early alcohol consumption, especially in the form of binge drinking, may be a precursor of other illicit drug use. [24] Many studies also demonstrate a link between alcohol excess and suicidal behaviours in adolescents, however the causal direction has not been well characterised. [25] These are compelling arguments that demonstrate not only a deleterious effect of alcohol, but also a clear correlation between minimum age legislation and outcome data.

Condition 2 - The power of the law

Despite certain experimental shortfalls, the overarching trend across neurodevelopmental, road safety and behavioural data seems to support this notion of 18-21 year-olds being particularly vulnerable to alcohol. If we accept this to be true, then the second key burden of proof relates to whether an elevated age gap actually does translate into a reduction in early-age alcohol consumption. Some critics argue that higher age restrictions in fact drive alcohol use underground and lead to more dangerous patterns of consumption. [26] In other words, age-21 laws do not allow adolescents to learn safe drinking practices within a family context, instead forcing them to experiment

independently, albeit at a later age. However, the data from large-scale European studies comparing adolescent drinking behaviours in the EU and US strongly suggest otherwise. The European School Survey Project on Alcohol and Other Drugs (ESPAD) found that a greater proportion of 10th-graders in Europe had consumed alcohol within the past 30 days (33% in the US versus 80% in Denmark, 75% in Germany, 64% in France). [26] Furthermore, a higher percentage had been intoxicated before age 13 (8% in the US versus 25% in Denmark, 14% in Germany, 9% in France). Of course, it is difficult to disentangle the effect of legislation in each of these countries from the influence of culture and tradition. However, on the surface it would appear that countries with lower drinking age consistently show earlier exposure to alcohol in adolescence.

New Zealand data have demonstrated that youth several years below the legal drinking age invariably gain access to alcoholic products through older friend circles and siblings [27] – a phenomenon that Tambourou et al. refer to as the "trickle-down" effect. [1] Evidence suggests that an upward shift in the legal drinking age not only reduces the number of 18-21 year olds consuming alcohol, but also significantly reduces the likelihood of 15-18 year olds acquiring it. In summary, the evidence supports the hypothesis that legal restrictions do translate into community practice.

Condition 3: A balancing act

Having satisfied the first two conditions, we arrive at the third and most challenging question: does the negative impact of alcohol amongst under-21s outweigh their personal autonomy as legal adults? Tangled up with this argument is the deeply-ingrained cultural idea that alcohol consumption is a mark of adulthood, a rite of passage. By instituting age-21 laws, the state would not only be removing personal autonomy, but also stamping out cultural aspects of the coming-of-age tradition. Is this fair, is it necessary, is it overly paternalistic? There is some evidence to suggest that raising the minimum legal drinking age causes a 'reactance phenomenon' where underage individuals drink more in response to the imposed restrictions. [28] However a large meta-analysis by Wagenaar et al. disputes this finding, demonstrating amongst 33 studies from 1960-2000 a strong inverse relationship between minimum drinking age and alcohol consumption rates. [29]

In spite of these data, there remains the fundamental philosophical issue of whether it is equitable to impose a blanket regulation across all under-21s when the negative statistics are driven by a small minority of excessive alcohol drinkers? Ultimately, these are questions of political philosophy more than clinical data – to what extent should the state protect individuals from themselves? There are no easy answers. This is a situation where public opinion must shape government policy.

An individualised system

One key problem is that public policy cannot take into account the diversity of the target population – with 18-21 year olds varying significantly in maturity, family support, and risk-taking behaviour. Given this variability, one might consider a system where alcohol regulations are personally tailored. As a thought experiment, consider the possibility of "alcohol licenses" for individuals. An 18-year-old might be required to pass a written examination on content similar to the current *Responsible Service of Alcohol* syllabus. There could be a point system, with points lost and licenses potentially revoked for alcohol-related misdemeanours. Perhaps even a provisional license system (like L- and P-plates) restricting the type and quantity of alcohol that could be purchased by youth. This would require a large bureaucratic infrastructure to support it; however it may be one option for creating a smoother pathway from adolescence into responsible alcohol use.

Conclusions

Tambourou et al. conclude their article with a call-to-action for a multi-level advocacy campaign in support of age-21 regulations. [1] However, perhaps the real value is in the dialogue more than the outcome. Ultimately, drinking age is an arbitrary number that does

not perfectly match the maturity levels of all individuals and certainly does not perfectly translate into alcohol consumption patterns. The important point is that society becomes aware of the risk of premature alcohol use, and that this knowledge becomes integrated into family education, peer dynamics, and youth culture. The real goal should be for adolescents to approach alcohol in a mature and sensible fashion. Regardless of where the Australian law ultimately settles, perhaps it

takes a high-profile legislative debate in order to bring this conversation into the spotlight.

Conflict of Interest

None declared.

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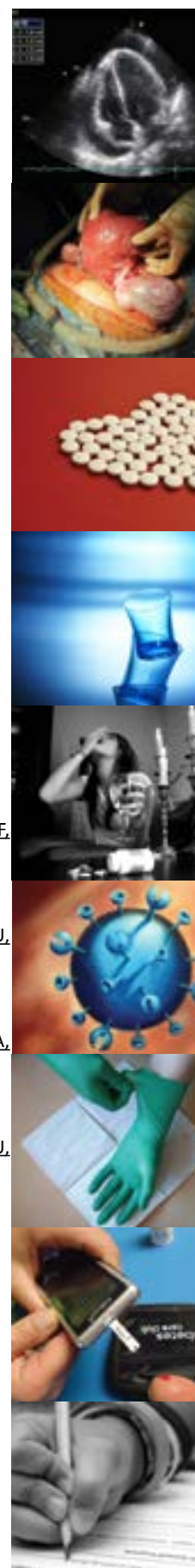
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