

Care Ethics at the Edge of Neonatal Viability

Infants born at the threshold of viability (22 to 25 weeks of gestation) present unique ethical and technical challenges. Care should always be compassionate and humane, maintaining the dignity and humanity of the infant as a person in their own right. The ethical dilemmas posed by the medical treatment decisions made on behalf of extremely premature infants can only arise in countries with sophisticated health care facilities, modern technology and health professional expertise.

Saving extremely low birth weight infants

The World Health Organisation (WHO) requires that all foetuses and infants delivered weighing 500 grams or more be reported in every country's national statistics.¹ In Australia, the criteria is 400 grams and/ or 22 completed weeks of gestation. When these extremely small and premature infants are born showing some signs of life, the decision whether to intervene with life-sustaining medical efforts or compassionate care may become imprecise and arbitrary.

In some countries, such as Italy, the law strongly protects human life especially that of minors. So strong is this law that resuscitating a premature infant is mandatory, even when the birth results from an induced late abortion.² In the USA the Bush administration recommends that doctors and hospitals must make every effort to save the lives of premature babies born alive after failed abortions.³ A disturbing factor in the discussion about extremely premature infants, in particular, is that abortion is legal in most Australian states almost up to the time when more and more extremely premature infants are surviving due to the availability of intensive care treatment.

Some, however, consider the extraordinary efforts expended in keeping extremely premature infants alive as 'a giant experiment'.⁴ Muraskas and colleagues consider health providers, newborns, and their families as being 'held hostage to biomedical technology' and despite medical, nursing and technical advances the morbidity statistics for Extremely Low Birth Weight (ELBW) infants, in particular, have not really improved apart from giving new meaning to the concept of 'viability'.⁵ Some neonatal nurses question the ethics of using potentially harmful technology on infants born at 24 weeks or younger who,

they believe, are kept alive in the interest of science rather than in the interest of the child and their family.⁶

Facts about ELBW outcomes

While survival rates of infants born at between 23 to 25 weeks gestational age have marginally improved in recent years, they do experience a high rate of serious morbidities in the Neonatal Intensive Care Unit (NICU). One study reported only 17% of 4172 infants born at a mean gestational age of 23.3 ± 2.1 weeks surviving to discharge.⁷ An Australian study suggests that survival can be up to 35% in this age group.⁸ The short and long-term cognitive and neurological development of infants born between 23 to 26 weeks' gestation continues to be a concern.⁹

Marlowe and colleagues reported on follow up at 30

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months and at school-age, of infants born at 22 to 25 weeks gestation in the United Kingdom and Ireland in 1995. Initial survival to discharge was 1% at 22 weeks gestation, 11% at 23 weeks, 26% at 24 weeks, and 44% at 25 weeks. At 30 months the infants were assessed for disability, defined as severe (indicating dependence on caregivers), moderate, or mild. There were 22% of children found to have a severe disability, 24% a moderate one and 34% mild. Of those children with severe disability at 30 months of age, 86% still had moderate to severe disability at 6 years of age. The rates of survival without disability at 6 years of age were none at 22 weeks, 1% at 23 weeks, 3% at 24 weeks, and 8% at 25 weeks.¹⁰

Treatment decisions and dilemmas

Opinions are divided about whether infants born at the edge of viability should be actively resuscitated if born alive. Some make a distinction between withholding treatment and withdrawing treatment, with the former being seen as a more acceptable moral option by many – though bioethically this distinction is not made. Yet the balance about whether to treat or not treat extremely premature infants probably tips towards actively treating these infants. Providers usually defend this by citing reasons such as perceived obligations in the face of an uncertain outcome, parental wishes and fears about legal liability.¹¹ J Singh and colleagues suggest that ‘the vast majority of infants in the NICU are admitted for a “trial of therapy”, tacitly or explicitly agreed on by their doctors and parents’.¹² But while the right choice is not obvious, neither is consensus about options which seem reasonable.

Health professionals and commentators who are involved in the provision of care to premature and ill newborns often suggest that various ethical principles are useful to guide decision making in regard to withholding or withdrawing treatment. But for parents making these same decisions the question of ethics is not paramount. Most parents want to believe providers offer the option to withhold or withdraw treatment because they not only care but also respect the parents’ wishes.¹³ However, health care professionals must recognise that their attitudes toward saving ELBW infants may differ from those of parents who may believe that attempts should be made to save all infants.¹⁴

Whilst the literature suggests that parents are usually involved in major treatment decisions, especially end-of-life decisions, a finding from Norway was that parents do not necessarily want the final word in decisions concerning their infants’ future life or death. They prefer the burden to be carried by the medical professionals.¹⁵ Research from the USA found that when disagreement about resuscitation decisions existed, doctors always thought parents preferred more aggressive resuscitation, and identified parents as responsible for the increased amount of treatment at delivery.¹⁶ Parents need realistic information such

as what is known about the short and long-term morbidity associated with ELBW infants. Given that many of these infants are born too quickly to make immediate informed decisions, parents may need time to consider their options or seek counsel from their family, friends or religious advisers after the infant is born. Clinical ethics committees may be another avenue to guide families and staff.

Parents are influenced by the quality of communication between care providers and family. Medical staff frequently mention three communication challenges in the NICU: parents unprepared to consider long-term implications of their baby’s condition; parents craving information...(but)...having limited capacity to absorb it; and parents questioning decisions that the physicians believed were settled.¹⁷ Ironically, parents of imperilled infants quite often consider that physicians lack communication skills. Parents particularly value clinicians who ‘treat them as parents’ and identify nurses as the central figures in setting the context of various ethical dilemmas that arise.¹⁸

Health professionals attitudes and experiences

A study exploring the attitudes of Australian neonatologists and nurses towards the resuscitation of extremely premature infants showed that 22% of the surveyed neonatologists would occasionally resuscitate at 22 weeks gestation while none of the nurses would. At 23 weeks gestation 23% of neonatologists would resuscitate but only 6% of nurses would. Neonatologists were more optimistic than nurses about survival of infants without major handicap.¹⁹ Nurses are generally more conservative about treatment decisions regarding ELBW infants.²⁰

Nurses who believe they have a higher level of influence in their practice environment are more likely to be involved in resolving ethical dilemmas but may believe they are limited in their ability to influence patient care.²¹ There is evidence that nurses may experience moral distress reasonably frequently when working with extremely premature infants.²² Moral distress is a process that involves recognition that a decision is difficult to act upon and can occur in a number of contexts including performing procedures one is opposed to.²³ Those who work in NICU environments presumably understand much about grief and bereavement.²⁴

Uncertain future

Recently, in the Netherlands, Verhagen and Sauer proposed what they term ‘The Groningen Protocol’ – a guide to when euthanasia may be an option for severely ill infants, though it is not legally permitted in this age group in their country or indeed any country.²⁵ Hastening an infant’s death via a lethal dose of medication is both illegal and immoral. Fortunately this extreme view is not widely

supported. In January this year Pope John Paul II urged doctors and authorities in the Netherlands to reconsider their stance on euthanasia.²⁶

With the advent of new and improved medical technology the profile of infants needing intensive care following birth has changed. With more premature infants surviving to discharge, the challenge continues to reduce the short and long-term morbidity associated with ELBW infants. Whilst not all infants needing intensive care fit in this category nor need extensive or long-term care, it is the ELBW infants who are overly represented in terms of ongoing medical, physical cognitive and behavioural problems. Much is still unknown about the long-term outcomes for these infants.

In developed countries the community appears willing to bear the costs associated with providing care to those born at the edge of viability. Public debate on the issue of whether there should be a gestational age limit for resuscitation has been suggested.²⁷ The way scarce health and welfare resources are shared does not always seem fair to certain groups. It appears that making definitive decisions about allocating and providing extraordinary care is often a hasty, frequently heroic and generally ad hoc process. But at all times, care should be about alleviating suffering and preserving the humanity and dignity of every individual regardless of their age and physical, intellectual and behavioural capacity.

ENDNOTES

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Health Care, Experimental Therapies, Research and Ethics

This general article discusses the basic duty of reasonable care of the health of human persons in the light of the ethical use of experimental therapies along with their risks as well as the ethical participation of human subjects in non-therapeutic experiments or simply human research. It does not deal with systematic human research and the responsibilities of Human Research Ethics Committees as outlined in the Australian National Statement on Ethical Conduct in Research Involving Humans.

In health care, it is important to remember that we are dealing with human persons, either as moral agents or as moral subjects of experimentation. Human persons are endowed with an absolute intrinsic worth in as much as they are rationally self-conscious, intelligent and free, capable of moral activity and of enjoying happiness -- even for eternity. Furthermore, human persons have a unique psychosomatic unity, constituted by the human spirit, or soul, actualising matter so that the biological, physiological and psychological dimensions form one human being, a single subject of human existence. It is true to say that the human person both has a body and is a corporeal being. The human person is conditioned by the requirements of human nature biologically, physiologically and psychologically for well-being, action and proper functioning. The human person forms such an integrated whole so that no one part, organ or function may be considered or treated in isolation from the rest, without regard for its total significance, both personal and interpersonal.

Persons are ends in themselves, subjects and not objects, and consequently cannot be reduced to mere means for the benefit of others. Each person has an inviolable dignity and value that transcend the social order and the requirements of the temporal good of the community. However, on account of their social nature persons have a duty to positively promote the good of others, persons are to some extent subordinated to the common good without being reduced to mere means status for its achievement.

Duty of care for one's health

We have to use our freedom wisely and responsibly to utilise natural resources to promote our own health and that of others. We are morally bound to take reasonable care of our health: from pursuing a healthy lifestyle and eating habits to seeking therapies for ill health from qualified health professionals when required. This is a personal responsibility of competent persons. As Catholic Health Australia says:

The primary responsibility for safeguarding and maintaining one's health so far as that is reasonable belongs to each person in his or her own right.¹

We are also bound to avoid intentional, and as far as possible, unintentional harm to our own or others' health. Alcohol may be responsibly consumed, but not to excess to the point where one's rational self-control is compromised or one's health is harmed. Drugs may be taken according to the right dosage provided they are prescribed by a medical practitioner for the person concerned. It is of the utmost importance to avoid taking mind altering substances which could impair one's capacity to act in a morally responsible way or even change our personality for the worse. It would be worse if the risks involved include the possibility of permanent damage. Vaccinations and/or immunisations may at times be required and we should be on our guard against being infected by food poisoning, tetanus, HIV, hepatitis B or C etc.

Medical staff are bound to provide all reasonable assistance, advice, and safe, reliable therapies. Vulnerable patients need more care and Catholic Health Australia warns that they 'may need to be protected from pressures which lower their self-esteem or encourage self-abandonment.'²

This will require mutual trust, responsible cooperation in agreed treatments, professional confidentiality and service, a reasonable sharing of all relevant information regarding one's illness and likely therapies, along with their potential risks. The dignity of the human person requires respect for the conscientious decisions of both patients and health care professionals in providing health care services, especially where an experimental therapy may be involved.

Experimental therapies and risks

Though there is always an element of doubt in the outcome of driving a car down the street, or administering a standard drug for the cure of an illness or the relief of painful symptoms, one would not count any of this as experimenting with humans. One has recourse to an experimental therapy when the standard therapy has failed, is

unable to be administered on medical grounds or is simply unavailable. To be morally justified in applying an experimental therapy, ie one that is deliberately undertaken knowing that its therapeutic outcome is not yet certain due to insufficient research, in addition to the moral requirements of any therapeutic intervention, both the doctor and the patient would have to be satisfied that the desired cure or benefits to the patient are worth the risks of harm or discomfort involved, compared to the likely outcome of the available standard therapy. Naturally we are dealing with prudential judgements, where the assessment of the risks involved or the desired benefits could vary from one health professional to another. This is unavoidable, but decisions still have to be made following thorough assessment and the full truth of the situation is to be made clear to the patient. This need not be done with all the accuracy of detail possible in medical terms. One can only expect reasonably adequate information to be made available in lay language. It is natural enough for the patient to rely heavily on the judgement of the doctor for a final free and responsible decision to accept the proposed treatment. One could very well be swayed by the knowledge that the therapy could also provide valuable information that would be beneficial for others. It goes without saying that every procedure would need to be scientifically guaranteed, devoid of any unnecessary dangers and well beyond the necessary stage of experimentation with animals.

In the more serious cases where there is a risk of death or loss of consciousness for a prolonged time, reasonable warning would need to be given to the patient to allow enough time for reflection and deliberation on the balance of benefits and risks, bearing in mind some may wish to consult a family member or another personal adviser, eg. a chaplain, prior to making a free and responsible decision.

Experimental therapies are adopted primarily for the medical benefit of the patients concerned (exclusively so in the case of incompetent patients) and only indirectly and incidentally for the benefit of the wider community by way of the increase in scientific and medical knowledge gained. After free consent is given, one still retains the right to withdraw from an experimental therapy at any stage. The purposes of therapeutic experiments include diagnosis, cures or the alleviation of pain.

Incompetent patients

In the case of incompetent persons such as children who are too young to understand the issues, the parents are to make the informed, free and morally responsible decisions in the best interests of the health of their children and not of the broader community. One may volunteer to assume additional risks for oneself for the benefit of the community, but not on behalf of children who are unable to make responsible choices for experimental therapies

that may involve risks of significant harm.

Human research

Ethically there are more difficulties when we consider medical research or non-therapeutic human experiments. Their purpose is not to cure, but to increase medical or scientific knowledge or to improve the practice of medicine by developing new therapies, devices, nursing methods and especially new drugs. The fruits of such research will be of benefit to the medical profession and the community at large, but will not directly benefit the human subjects involved. The National Statement on Ethical Conduct in Research Involving Humans rightly says

When conducting research involving humans the guiding ethical principle for researchers is respect for persons which is expressed as regard for the welfare, rights, beliefs, perceptions, customs and cultural heritage, both individual and collective, of persons involved in research.³

There is no special moral problem for adult moral agents in freely consenting to take part in research or non-therapeutic experiments provided there is no risk, or only a negligible risk, of serious harm resulting to themselves. They would need to obtain beforehand sufficient and adequate information about the nature, purpose and possible effects of such experiments. The very low risk of harm could be justified by the potential benefits of the research. We justify the low risks of driving a car by the benefits gained in daily life by the convenience of having cars.

The case is different if a serious risk is involved. I agree with Pope Pius XII, when referring to a research participant, he said:

He cannot, therefore, submit himself to scientific experiments or practices that entail serious harm or threaten his health. Still less is he authorised to attempt any experiment, which according to authoritative information, may involve mutilation or suicide. The same must be said of male and female nurses and of anyone who may be disposed to give himself the therapeutic research. They cannot submit to such experiments⁴.

One may not volunteer for such risks, and much less may state authorities or anyone else coerce individuals to submit to dangerous experiments. However, I would not exclude the morality of persons genuinely volunteering to undergo lesser risks to health and life for the advancement of scientific knowledge in an area that would undoubtedly be of great benefit to the community. Such risks are accepted with the necessary precautions in the mining industry, the test-flying of new aircraft, the building industry and the protective services such as the police and the fire brigade. The taking of a reasonable risk of harm or a sacrifice for the common good would not be

immoral. Referring to clinical trials, Catholic Health Australia states:

The use of placebos, or non-treatment control groups, is acceptable only if they are necessary for the purposes of the research, do not deprive the patient of available, beneficial and needed standard treatment, and do not place the patient at risk of harm.⁵

It would be imperative to guarantee that no undue pressure was being exerted on the freedom of choice of subjects who were vulnerable or in any way dependent persons in positions of authority, eg. people with some intellectual impairment, students of the medical researchers, soldiers or prisoners. Acts entailing some degree of heroism may be chosen freely, but one is not morally obliged to choose to participate nor may one be forced or pressurised into participating in risky experimental research. Participants should not risk harm to their personality, or impair their ability to behave normally or to act in a free and morally responsibly way.

It goes without saying that those responsible for incompetents may not decide to breach their trust of responsible care towards their charges by consenting to allow them to be subjected to experimental research of any kind that involves risk for their health or lives. I see no difficulties in allowing research experiments when no risks at all or only minor insignificant risks are involved. This would be a responsible exercise of their trusteeship for the benefit of the community, particularly if such research can only be done on infants or children for the eventual benefit of the same class of incompetent persons. Still, to guarantee impartiality and objectivity of judgement in assessing the possible risks, such projects should be submitted to a competent independent panel of review for clearance from any possible long term harmful consequences.

It would be immoral to remove tissue for medical research or transplantation from a live fetus, be it viable or even pre-viable. This intervention would clearly not be for the benefit of the fetus since it would bring about its death immediately.⁶ It would be different in the case of a recently

miscarried fetus, provided the informed and free consent of the mother was obtained. There would be no special moral problem involved in obtaining fetal tissue from a deceased fetus.

Likewise it would be immoral to use tissue obtained from aborted fetuses to the extent that this practice would involve collusion, in the estimation of the community, with the deliberate loss of fetal life in the first instance, notwithstanding protestations to the contrary. Catholic Health Australia rightly says:

Research is never to be undertaken on an embryo or a foetus, or on tissue from an embryo or a foetus, that has been procured through deliberate abortion.⁷

One could not, without moral culpability, profit from another's wrong doings, be it theft, bribery, tax evasion, blackmail, the earnings of prostitution or violation of professional confidentiality of a State Government -- not even for the best of motives. It would be even worse to persuade a woman by financial inducement to postpone her abortion until the pancreatic tissue of the foetus was large enough to warrant harvesting it.

All forms of experimental therapies and human research are to be directly at the service of persons and indirectly of the community, without anybody being unduly subordinated to them.

ENDNOTES

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² *Ibid.* 43

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⁷ *Ibid.* 52.

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Review of Human Embryo Research & Cloning Laws

A former Federal Court judge will head an independent review into stem cell and cloning laws, moving Australia closer to decisions about the use of embryos in medical research' The Age 18/6/05

In order to make your submission to this committee the book *Stem Cells Science Medicine Law & Ethics* published by the Caroline Chisholm Centre for Health Ethics will be invaluable. Price including postage: \$20.00.

In order to purchase a copy contact Alice at the Centre . For Contact details see Page 12.

Integrity in Clinical Research

The progress of medical science has become increasingly dependent on the pharmaceutical industry and this seems to have direct implications for public health. The link between medicine and the industry has directly affected the way that medicine is practiced and also the quality of clinical research. In an increasingly globalised world, the quality of medical research and practice should be dictated by ethical standards and not by market forces.

Introduction

Medicine and the pharmaceutical industry share common interests, with constructive relationships giving clear benefits in healthcare. Both have an interest in promoting the use of effective medications and furthermore, developing new technologies and pharmaceuticals through the ethical conduct of clinical research. Cooperation can and does enhance healthcare. There are, however, well documented risks. These arise primarily from the divergent interests of industry on the one hand, and clinicians and researchers on the other. While the interests of healthcare professionals should properly be patient and community welfare, the primary interest of industry is clearly to maximise profits for shareholders. Neither of these aims are unethical as such: it is where they intersect that problems can arise. One of the major points of collision is that of the conduct and reporting of clinical trials.

Conflicts of interest

While it is not in the public interest to proscribe relationships between medicine and industry, it must be acknowledged that there is an increasing 'enmeshment of researchers in the for profit sector and a shift to research conducted in private rather than in the setting of the academy.¹ In recent times this trend has accelerated---innovative technologies and product development has been left to the marketplace, not to traditional institutions such as Universities, public hospitals and government departments.² For drugs and vaccines, this is the pharmaceutical industry, which, in 2002, spent more than US\$32 billion on research and development in the US alone.³ This has undoubtedly reaped benefits with virtually all of the new drugs developed in the past 60 years---drugs that have transformed medicine---having been either developed or manufactured by drug companies.⁴ Large pharmaceutical companies are increasingly funding clinical research, with over 90% of drug trials being conducted by industry.⁵

Legitimate concerns have been raised that clinical research is becoming increasingly vulnerable to pressure from industry sponsors. Presently, reporting adverse events during clinical trials is usually the responsibility of the sponsoring company. With large profits at stake, this may not be the best system as recent cases, such as Vioxx (see below), demonstrates. More comprehensive monitor-

ing by regulatory agencies such as the Therapeutic Goods Administration could minimise unwarranted influence, but to do this the government would need to spend more on ethical oversight. Furthermore, in Australia corporations marketing drugs and devices pay for ethical evaluation of their own trials; a situation which is hardly ideal.

Bias in reporting

Reported author affiliation with industry has now increased to 66% of clinical trials sponsored solely by industry. An increase in the percentage of clinical trials with author-industry affiliation has been observed for all journals and through all disciplines. This is of concern as the integrity of the research may be compromised by the sponsor of the trial. In the majority of published studies, clinical outcomes did favour the study drug.⁶ Indeed, a systematic review by US researchers found industry sponsored trials are four times as likely to have outcomes favouring the sponsor than are studies funded independently.⁷ In other words, systematic bias favours medical products which are produced by the study sponsor.⁸

Meta-analyses are the gold standard in reviewing efficacy and safety of new drugs and medical devices. However, suppressed or delayed publication of data may bias the results of meta-analyses, resulting in incorrect risk-benefit profiles for drugs. Such bias in publication can unfairly distort the picture and impair the clinician's judgement when prescribing. This unethical practice can not only endanger the patient's welfare but undermine public confidence in medicine.

Integrity in clinical research

Publishing findings in a selective manner is not the only way research integrity can be compromised. Trial methodology can also be manipulated. Unethical tactics can be employed to give sponsoring companies the results they want, including comparing the new drug with a placebo rather than a standard evidence based treatment, comparing the new drug with an inappropriate existing drug or even with too low a dose of the existing drug.⁹ A European study analysing placebo controlled studies of selective serotonin reuptake inhibitors (such as Prozac) found a literature compromised by multiple and selective publications showing significant drug effects by ignoring some studies and highlighting others.¹⁰

These tactics are clearly not in the public interest as the recent case of Vioxx demonstrates. The alleged failure of Merck, a pharmaceutical giant, to release damaging data about cardiac risks associated with its blockbuster pain drug has prompted US congressional hearings with charges that the company knew of the risks earlier but failed to disclose them. This scandal has been followed by another in the UK. Representatives from Wyeth have been publicly censured for questioning a safety warning released by the government regulatory agency. Furthermore, Wyeth misquoted official guidance on the treatment of depression so as to favour the drug.¹¹ The agency has made it clear it would not tolerate misleading advertising material when it comes to safety issues. 'In naming and shaming Wyeth, we hope this message will be clearly understood by all involved in medicines.'¹²

Such practices are contrary to sound research. Furthermore, they endanger public health and as such are clearly unethical. Although it is not clear how widespread these practices are, there are some steps that could be taken to eliminate them.

Personal integrity

It is of utmost importance that researchers themselves have a high degree of personal integrity. Not only ought they be dedicated to the quest for objectivity and the truth, but they must be imbued with a strong commitment to the demands of justice, fairness and the need to avoid harm to research participants. Such standards ensure clinical research will be not only honest, in design and in its conduct, but open, scientifically justifiable and safe to conduct.

The importance of research integrity has been recognised by the Commonwealth. The peak body for regulating human research in Australia, the National Health and Medical Research Council, has published the *National Statement on Ethical Conduct of Research Involving Humans*. In this document they require four key guiding ethical principles in human research, one of which is Research Merit and Integrity. Its importance is made abundantly clear:

1.1 "The guiding value for researchers is integrity, which is expressed in a commitment to the search for knowledge, to recognised principles of research conduct and in the honest and ethical conduct of research and the dissemination and communication of results."¹³

Further steps

It is easy to focus blame on researchers or the drug companies, but the case is not as straightforward as that. As a public corporation whose purpose is to discover and develop medical products that meet demands, Merck and other companies, are obliged to protect confidential information and intellectual property, including aspects of the

design of clinical trials and, at times, the very existence of certain studies.¹⁴ Several leading medical journals, including the *British Medical Journal*, have pressed for a requirement that all clinical trials be placed on a public registry, a proposal endorsed by the Australian Medical Association (AMA) and the WHO. A comprehensive, easily accessible registry is certainly needed, but publication of trial protocols is also in the public interest. Although this is to be applauded as it increases transparency in clinical trials and their outcomes, whether positive or negative, it does directly conflict with commercial confidentiality.

Furthermore, journals are late in a research process that takes many years of planning, execution, and interpretation. Care in weeding out drug company influence and protecting patients ought to begin from the outset. Human research ethics committees (HREC) have a vital role in ensuring that new clinical trials are both ethical and scientifically justifiable. A clinician who has ties to the company sponsoring the trial should not be present at a HREC meeting while deliberations on that trial are underway. The same applies to a clinician whose own trial is being considered. In this way, conflicts of interest are minimised during ethical appraisal. And all other members need to be aware that drug development and marketing is a multi-billion dollar industry, where financial interests influence the design and planning of clinical trials.¹⁵ Another proposal, contained in a recent report released by the UK House of Commons Health Committee, has much merit. It has recommended that medical students be educated about industry marketing, adverse events and the ethical conduct of clinical trials.¹⁶

There is, however, a need for more than just improved registering and monitoring of industry sponsored clinical trials. This problem goes beyond the pharmaceutical industry. A recent empirical study showed that 62% of randomised controlled trials deviated from their research protocols in reporting primary outcomes, including those funded by government research councils, reputable charities, and universities.¹⁷ For both harm and efficacy data, outcomes were more likely to be reported if they were statistically significant.

Another avenue for improvement may be professional bodies and governments themselves. Some Commonwealth authorities and professional medical organisations are recommending new or revised policies regarding financial disclosure, conflicts of interest and arrangements between industry and clinicians. Indeed, the Royal Australasian College of Physicians is currently revising its guidelines and most other colleges now have policies in place.¹⁸

It appears that research integrity, both for individuals and corporations, is not always adhered to, although the extent of such breaches is unknown. What is clear is that all

those involved in clinical research must endeavour to eliminate bias and any other practice that compromises research integrity. What is at stake is not only patient welfare, but the reputation of the whole research sector in healthcare.

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Ethical Issues in Complementary and Alternative Medicine

Complex ethical and legal issues have arisen as the risks and benefits of CAM and its interaction with conventional medicine become better understood.

Definition

'Fringe', 'Complementary', 'unconventional' or 'alternative' medicine are all umbrella terms for a vast range of healthcare modalities, collectively becoming known as CAM--Complementary and Alternative Medicine. From relatively new modalities (eg, massage therapy and magnetotherapy) to ancient skills of an initiated community (eg, yoga), and traditional practices that are mainstream in some cultures (eg, traditional Chinese medicine), CAM includes a wide spectrum of healing strategies that derive from systems radically different from the Western tradition.

The definition used by the National Center for Complementary and Alternative Medicine (USA) is 'healthcare practices that are not an integral part of conventional medicine. These practices may be grouped within five major domains: alternative medical systems; mind-body interventions; biologically-based treatments; manipulative and body-based methods; and energy therapies.'¹ This plethora of modalities all revolve, in one way or another, around the principle of *vitalism* — that human beings, in-

deed all life forms, are nourished by a vital force, which is at once different from, and greater than, physical and chemical forces. Such a position 'contrasts with materialism, which holds that disease can be explained entirely in terms of materialistic factors (usually biological ones in the case of biomedicine), so there is no need to invoke vitalistic forces.'² Thus vitalism promotes a different philosophy underlying well being, healthcare and the role of the practitioner. This is what fundamentally distinguishes CAM from conventional medicine.

Popularity

Due to the pre-eminence of science and biomedicine in Western healthcare, the precepts on which it was founded are typically accepted as more accurate and true than modalities originating from other traditions. Indeed, 'the practitioners and scholars of the western biomedical tradition have gained social authority as the arbiters of truth as far as medical matters go.'³ But the *status quo* has begun to shift somewhat. While the causes of the rise in demand for CAM are largely unknown and little researched, the increasing popularity of CAM products and services within Australia and other nations appears to be primarily driven

by a grassroots social movement.⁴ What is beyond doubt is that CAM is now so well entrenched within mainstream society that a majority of citizens now either use CAM or are open to its use. Government and community surveys, conducted both here and abroad, show that around half of the public report using CAM treatments.⁵ To put that in dollar terms, Australians are estimated to spend almost twice as much on CAMs (\$621 million per year) than their contributions to pharmaceuticals, and a further \$309 million on CAM practitioners each year.⁶ And this trend is set to continue, with the international market for CAM products estimated to be expanding at more than 15% per year.⁷

Among the reasons given for this exponential increase in CAM popularity are:

- resistance to traditional authorities, such as doctors, and seeking greater levels of individual control and empowerment over their lives (a trend facilitated by the Internet);
- faith in the ability of science and medicine to solve the problems of living has declined, while alternatives appear to have more to offer;
- the perceived inability of orthodox medicine to satisfy demands for compassion, equity and efficiency;
- the reaction to the perceived evils of 20th-century science and materialism, with a turn to more “natural” ways of living; and
- societal trends toward individualism, in contrast to the perceived anonymity of scientific, population-based care.^{8 9 10}

Safety--consumer protection

Despite differences between CAM and the Western medical tradition, the ethical criteria for treating patients remain the same. In addition to informed consent, treatments must be safe and efficacious to be ethical acceptable. All products for human medicinal use must be placed on the Register of Therapeutic Goods.¹¹ Substances used in complementary medicines are classified as *listed or registered* and are assessed for safety and quality by a federal body, the Therapeutic Goods Administration (TGA).¹² Products can be *listed* provided they contain substances regarded by the TGA to be of low public health concern. The formulations have to be manufactured by a TGA-licensed manufacturer following a recognised code of Good Manufacturing Practice.

Registered products, on the other hand, are more rigorously scrutinised, and contain ingredients that are restricted by Federal Standards,¹³ have efficacy claims which are more substantial or are specified by the TGA as being of some health concern. In order to be registered, appropriate documentation outlining clinical trial work must be submitted to a sub-committee of the TGA. This is costly and few CAM products have been evaluated in

this way. Thus most CAM products are not exposed, either before or after market release, to the same level of scrutiny as pharmaceutical medicines. Part of the reason for this is that few CAM preparations can be patented, so they cannot generate anywhere near the profits that drive the pharmaceutical market.

Serious adverse events

Despite the perception that natural products are not dangerous, there is evidence to suggest that CAM use is not without risk. A large review conducted by the National Poisons Unit (London) showed that out of all complaints, over 95% were related to natural products. While 77.7% involved vitamin preparations which usually contain some level of natural supplements, 19.3% resulted from taking herbal extracts and other natural products.¹⁴ Serious reports of adverse reactions to CAM products have also surfaced. For example, both here and abroad liver toxicity has been associated with kava extracts, which had been indicated for the relief of anxiety. A review of recent cases concluded at least 24 were directly attributable to kava, with 8 of these patients requiring liver transplants.¹⁵ This has led to the banning of kava derivatives in many Western countries and clearly shows that, like medicine, problems can arise with inappropriate use.¹⁶

Reporting of adverse events is as essential for CAM products as it is for pharmaceuticals in providing long-term surveillance, thereby ensuring public safety. In Australia, reporting of adverse effects of any medication, whether alternative or conventional, is usually undertaken by a medical practitioner. But self-administered CAM products escape such scrutiny and even experienced practitioners, CAM or otherwise, may miss associations between complex preparations and symptoms. Furthermore, there is very little known about the effects of interactions between CAM and conventional medicines in the body. This is why there have been calls by authorities such as the Australian Medical Association (AMA) advocating the integration of CAM with conventional medicine. To be promoting or giving dangerous products is clearly unethical. More attention is now being given to extensive research, and the safety of CAM therapies are increasingly being evaluated in randomised trials and systematic reviews.

Efficacy

Alternative modalities in healthcare usually become particularly significant to patients where the burden of illness is substantial. This can include cases where there is no proven conventional therapy available, where the therapy that is available is invasive or associated with minimal benefit or major toxicity, where complementary therapy may be of benefit and has few risks and where the patient has expressed an interest in, or preference for, alternative therapies.

Listed alternative products do not have to satisfy the same levels of evidence as *registered* ones, which are assessed more rigorously because they make more substantial efficacy claims.¹⁷ But even this approach is problematic because many of these claims are not definitive. Efficacy data have to be held by the manufacturer of such products and can be called on at any time by the TGA or the Australian Competition and Consumer Commission. However, the TGA only carries out random checks, and prosecution for fraudulent activity is relatively rare.

With many preparations, particularly those being listed, not being thoroughly tested for efficacy,¹⁸ Australians may be inadequately protected from some unscrupulous practitioners within the CAM industry. While such products may be harmless, it is still questionable to give treatment or products when there is negligible or simply no benefit. And it is patently unethical to take advantage of the most vulnerable in our community, such as those with incurable or fatal diseases who may understandably seek desperate measures. Furthermore, such behaviour jeopardises the reputation of the industry as a whole. Perhaps health departments, from both State and Commonwealth, should be doing more to regulate and more importantly, warn the public about bogus claims.¹⁹

Legal issues

Increasing popularity in CAM has recently focussed attention on the proper role and legal responsibilities of clinicians in an expanded healthcare field. In particular, there has been concern over whether a doctor is liable for failing to adequately inform patients of alternative treatment options. A doctor's common law obligation to provide accurate information may well entail that the clinician has a duty to provide information about CAM therapy where such information would be material to a particular patient. While there is contention over what exactly constitutes 'material' in this context, it would commonly mean what a reasonable person would hold to be significant, given the patient's circumstances. Further, clinicians are ethically obliged to provide patients with enough information to make adequately informed healthcare decisions and valid consent to treatment. This information ought to include the risks and benefits of any relevant alternative treatments, as a recent case involving a doctor's referral to a chiropractor demonstrated. The injured patient successfully sued the doctor in the NSW Supreme Court which ruled that it was no defence that the injury was inflicted by another practitioner as the referral was deemed inappropriate in the first place.²⁰

Possible Solutions

The CAM revolution is upon us. Teaching of basic CAM in medical schools, Government reviews, new journals, sections dedicated to CAM in medical journals, and in-

creased media coverage are all evidenced throughout the Western world. Because of the exponential uptake of CAM, health departments and legislatures are taking steps to ensure that safety, competence and training are accorded the importance they deserve. Professional and regulatory responses have also emerged. But the proper regulation of healthcare professionals requires more than peer review.²¹

Regulation

Regulation of CAM practitioners is primarily the responsibility of the State and Territory governments. All state jurisdictions currently have legislation for registration of chiropractors and osteopaths.²² Victoria is the only Australian state or territory to formally regulate Chinese modalities, requiring those using the title 'acupuncturist', 'Chinese herbal medicine practitioner' or 'Chinese medicine practitioner' to register with the Chinese Medicine Registration Board.²³ The remainder of CAM practitioners are only subject to varying forms of professional self-regulation. Naturally, as with clinicians, CAM therapists may also be investigated by healthcare complaints boards and, where damage can be shown, litigation through the courts.²⁴

Validation

Scientific evaluation of CAM health claims is seen by many in the field to be vital if convergence is to be accepted by the majority of the medical profession. The area is, however, both controversial and difficult. Federal resources to test the validity of the plethora of CAM modalities is difficult to obtain, with a minute proportion of research budgets going to CAM research, although several universities have now established laboratories for such studies.²⁵ Perhaps 'the CAM industry itself should do more with its considerable profits to provide research dollars, but there is much internal resistance to the double-blind, placebo-controlled "gold standard" of orthodox medicine.' Furthermore, examination of CAM products have shown great variability; standardisation is so poor that preparations might not contain ingredients noted on the product label.²⁶

Conclusion

Another major response is the emergence of integrative, or integrated, medicine which can be achieved in numerous ways. Firstly, doctors could seek training in popular CAM methods and products, such as acupuncture, traditional Chinese medicine or naturopathy. This presents challenges, however, as there is evidence that many conventional medical practitioners are unaware of, or resistant to, CAM modalities and the evidence that already exists for CAM. Secondly, CAM providers could practise in traditional medical centres. A third solution for doctors may be simply to learn as much as possible about CAM,

and to ensure their patients feel comfortable enough to discuss their use of CAM with them. Even the AMA's position statement on CAM expects that doctors should have some knowledge of CAM to properly inform their patients about therapeutic alternatives.²⁷

While government, the AMA and other professional associations appear to support the integration of CAM, provided it is evidence-based, such an approach has significant implications for CAM. Integration may actually lead to fragmentation, or worse, disintegration of helpful alternative therapies. 'By emphasising standardisation, efficiency and generality at the expense of communication and individualised care,' CAM practice may well be fundamentally changed and healthcare suffer as a result.²⁸

Overemphasis on evidence, regulation or integration fails to appreciate the substantial differences between allopathic and complementary medicine, including differences in the meaning of health and illness, in methods, language and culture and crucially in their relationship to science. There are no easy solutions or quick fixes--yet the situation obviously needs to be addressed so that healthcare can be more comprehensive and, in doing so, serve the public in the most beneficial way.

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