Commentary on Spriggs: genetically selected baby free of inherited predisposition to early onset Alzheimer's disease

I note with interest the controversy regarding a baby born free of an inherited predisposition to early onset Alzheimer's disease through the use of preimplantation genetic diagnosis (PGD). As the medical geneticist for the PGD programme for single gene disorders in Melbourne, Australia, I have seen many couples who have considered PGD for a wide range of genetic conditions. My observation is that many will look to PGD for "milder" conditions and adult onset conditions for which they are not comfortable to have traditional prenatal diagnosis and termination procedures.

An example of this is that in the last 11 years our unit has undertaken 13 prenatal diagnoses for Huntington's disease from nine couples, whereas in the two years that we have been doing it we have had six requests for PGD for Huntington's disease and three couples have already had IVF cycles.

I have a number of concerns with the argument that the woman should not have a child if using PGD because she is predisposed to Alzheimer's disease. Firstly, do the commentators believe that the couple should not have a child by natural means because of this fact? If so, in this case, what length of time should be gone to prevent the woman becoming pregnant by natural means? If the commentators who make this argument agree that it is not appropriate to prevent couples where one is at risk of a genetic disorder from having children by natural means, then assisting them to have children not predisposed to a genetic disorder is in my view entirely ethically acceptable.

The concerns for the child of having a mother suffer from early onset Alzheimer's disease are that they will not have a mother to bring them up and the impact this will have. While members of the woman's family have developed disease in their 30s and 40s, this is by no means certain for the woman herself. The only other report of people with this mutation also had early onset Alzheimer's disease, but the numbers affected are very few, perhaps too few from which to draw a definitive conclusion about the exact age of onset for those with this mutation. For example the average onset of the Val171Ile mutation is 57 years. This is a mutation involving the same amino acid (valine at position 717) and the substitution is for a chemically very similar amino acid iso-leucine compared to leucine. If the destiny of this particular woman is to develop Alzheimer's disease in her mid 40s or beyond then her child will be an adult by the time she is severely affected. Even if we assume that onset of symptoms will be when the child is about 10 years old, the family are aware of this risk and can take steps to be prepared and put in place plans for this. Are couples with other sociological risk factors that put a child at risk of emotional deprivation prevented from utilising reproductive technology? In Australia at least, those who are from low income brackets or who use illicit drugs are not precluded from assisted reproductive technology, yet both these factors are associated with a number of poorer outcome measures for children.

Finally, PGD is a major undertaking for families. It is a protracted, expensive, and very stressful process and ultimately there is no guarantee that a child will be born through it. Many couples who consider utilising PGD do not go through with the process for these reasons and choose other reproductive options, including traditional prenatal diagnosis, and natural pregnancy with no intervention, or they decide against having children. Therefore families who undertake this process are generally highly motivated and, one intuitively feels that the resultant child is less likely to suffer social deprivation. This issue will only be resolved by long term follow up studies.

In conclusion, I believe that PGD is ideally suited to situations where families wish to avoid their child developing a particular genetic disease, but where they feel uncomfortable about terminating pregnancies. This includes late onset conditions such as neurodegenerative diseases and familial cancer syndromes, as well as early onset diseases that are considered relatively mild, such as deafness.

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References


Electronic submissions to the Journal of Medical Ethics

At the time of writing there appear to have been no electronic submissions to the Journal of Medical Ethics. It seems appropriate, therefore, to begin electronic correspondence with a consideration of some of the ethical implications of this new form of ethical dialogue.

I have posted this response to Kenneth Boyd's editorial on Mrs Pretty and Ms B as this article may provoke debate far beyond the medical and ethical establishment. This issue may be of tremendous concern to patients or their carers who are presently suffering in circumstances similar to those described. The electronic response forum of the BMJ has been in operation for over four years. An editorial in the BMJ on physician assisted suicide1 has attracted 125 responses at the time of writing. An important feature of electronic responses, particularly on items that generate a lot of debate, is that the contributions often refer to each other. These responses range from the scholarly and meticulously argued to distantly related. As both an avid reader of rapid responses to the BMJ, and a physician, I consider both sorts of contributions to be valuable, but increasingly feel uncertain about what my written response to them should be when I wish to enter into dialogue with the author. I feel on sure ground when considering the scholarly submission that is clearly intended as a contribution to a peer reviewed journal, and have no qualms about drawing up a response to point out its weaknesses. Equally, as a family doctor, I hope that I am able to approach distressing accounts of suffering with a degree of empathy. It is sometimes the case, however, that submissions clearly showing distress also contain dubious argument that any peer review process would deal with severely. "Where accounts of suffering alongside dubious arguments are posted from patients I personally feel squeamish about responding, finding myself caught between the roles of vituperative reviewer and empathic listener. As an editorial in the BMJ on the subject of electronic responses has noted: "We've begun to capture the opinions and experience of patients ... and publish just about anything that isn't libellous or doesn't breach patient confidentiality". I inevitably, such a broad range of responses will produce many that deserve to be challenged. Merely to ignore dubious argument implies that such opinions are correct. Furthermore, it is astonishingly easy to post an electronic response, and the process contains no warning that opinions expressed may be severely challenged. We should consider what the rules of debate on this Journal of Medical Ethics web site should be.

To prevent any misunderstanding, I wish to state that this response does not issue out of intense personal suffering, and that I am prepared for the most stringent peer review of its contents. Say anything in response, but please don't ignore me.

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References

Dr Lewis raises the important issue of what the rules of debate should be in electronic correspondence. An editor, I feel as if I am caught in the maelstrom of evolution. The web has radically changed the nature of debate and the presentation of information and knowledge. It is not clear to me how and whether it should be controlled. My general approach has been to let the experiment run in a free way and look at the results. Then it will be clearer what rules are required.

Electronic correspondence, for me, is different from scholarly debate. It takes advantage of the web’s accessibility to give people the opportunity to express their own views and to see the range of views on a particular issue. At present, the JME operates on the principle that it will publish electronically any response which is not libellous or harmful in other ways. Electronic letters which contribute significantly to the debate (such as Dr Lewis’s letter) may be selected for publication in the paper version of the journal.

The core business of a journal such as the JME should be the publication of scholarly articles which contribute to knowledge. But as a medical ethics journal, it should also be engaging and relevant to professionals and non-professionals. We have introduced a current controversy section which reports an issue of contemporary interest and we solicit non-professionals. We have introduced a casebook format entices the reader into a variety of perspectives that may include emphasi, bringing to bear, as it should, an analytical strategy lead to progressively deeper levels of understanding of the ethical issues, thus exposing “the heart of the matter”, along the way one is referred to books, chapters, and articles for further reading. As might be expected, Fulford’s notion that an explicit analysis of values is helpful in defining diagnostic concepts, that medicine is a recurring theme. Dickenson’s interest in informed consent (also in children), “moral luck”, and her feminist reconstruction of the question of the differential diagnosis of a man who appears to have a religious delusion, yet leads a very successful professional life turns “not on the facts about his experiences and behaviour, but on a series of value judgements”. The authors point out that the diagnosis of schizophrenia in the DSM-IV (a widely used diagnostic classification system) requires the criterion of “social/occupational dysfunction... below the level achieved prior to the onset”. Here a paradox is demonstrated: the evaluation of “social dysfunction” depends on values, yet the authors of the DSM-IV claim that the system was “grounded in empirical evidence”.

The reader is challenged to come to terms with the value related elements of the diagnosis of schizophrenia and related diagnoses. As with several other cases, the importance of a team approach is emphasised, bringing to bear, as it should, a variety of perspectives that may include elements of cultural formulation and the patient’s values.

Other chapters address teamwork and service organisation, and research ethics; a section on wider perspectives gives an international view; in an interesting chapter Fulford describes the basis for his belief that psychiatry can take the lead in bioethics, “providing lessons for medicine as a whole”. There is also a useful sample teaching seminar, showing how theory is put into practice.

The book will appeal to any reader who wishes to escape from the well-worn path of “four principles plus”. It is likely to be enriching to psychiatrists who feel that the DSM-IV and ICD-10 are constrained not so much by limitations of their science, but of their humanities. It provides thoughtful material for those interested in finding a way of resolving the tensions between physical medicine, psychiatry, and ethics. The book is a treasure trove of annotated bibliographies and very enjoyable to read.

S Louw

Ethical Issues in Palliative Care—Reflections and Considerations


This book is a collection of essays by a variety of specialists with a particular interest in palliative care. It contains seven chapters by six different authors.

The first chapter Why is the study of ethics important? is by Patricia Webb, a lecturer in biomedical ethics, explores the difference between the two and how they are related. She tells us that studying ethics encourages logical reasoning thinking in the face of difficult decisions such as allocation of resources, access to services, best care, clinical research, and rights to life. Webb reminds us that clinical guidelines may not be much help in the face of an ethical dilemma with no clear right or wrong answer.

The chapter called Care versus cure by David Hopwood, consultant in palliative medicine and writer on medical ethics, reminds us that care is concerned as much with the subjective feelings of the patient as with the physical disease, and aims to relieve suffering and improve quality of life. He emphasises that by sharing the reality of uncertainty (with patient, family, and colleagues) we can make more realistic decisions, and that an important role is played in sharing the power of doctors and patients.

Giving it straight—the limits of honesty and deception by Heather Draper, a lecturer in biomedical ethics, explores the difference between truth-telling and honesty, and between honest and dishonest selective truthfulness. “There is a sense in which we are always selective with the truth”, she writes and reminds me of the saying so useful in palliative care: “It is better to be a little dishonest if it helps to keep the patient going”. He emphasises that care is concerned as much with the subjective feelings of the patient as with the physical disease, and aims to relieve suffering and improve quality of life. He emphasises that by sharing the reality of uncertainty (with patient, family, and colleagues) we can make more realistic decisions, and that an important role is played in sharing the power of doctors and patients.

The chapter on Advocacy by Patricia Webb defines advocacy as “the role of one with expertise who is invited to negotiate on behalf of another”, and is an interesting analysis of the power differences between patients and professionals. She makes the point that “patients have little power to influence the nature of care provision unless a determined effort is made to reduce their actual and perceived vulnerability”. She also emphasises, however, that skilful communication allows doctors to be involved in decision making. With good team care few patients need an advocate, except those few who prefer to be very passive, or who are unable to make decisions, such as those with severe learning difficulties.

The next chapter, How informed can consent be? by Calliope Farsides, a senior lecturer in medical ethics, makes the point that it is often useful to consider consent not primarily as a legal concept but a moral one, and one that depends on the relationship between patient and carer and their trust, reciprocity, and beneficence, with mutual recognition of their duties and obligations. She goes on to look at the differences between...
Life and Death in Healthcare Ethics: A Short Introduction


This is a compact, nicely written book that provides a refreshing alternative to the utilitarian orthodoxy that dominates contemporary bioethics. There is currently a dearth of bioethical literature presenting what might be called a more traditional approach to medicine and health care. This contribution is a short and useful introduction to such an approach.

The book announces itself as being written with “both the general reader and students and professionals in medicine, nursing, law, philosophy and related areas in mind”. Accordingly, it assumes no prior knowledge of ethics. It gives a neat introductory overview of some ethical problems raised by reproduction, death, and dying. The issues considered include euthanasia and withdrawal of treatment, the persistent vegetative state, abortion, cloning, and in vitro fertilisation.

By beginning with an early chapter with a real-life case, Watt captures the interest of the reader. The case is introduced and discussed dispassionately. It is then employed as a forum and resource for managing difficult clinical dilemmas, with both philosophers and clinicians facilitating. In the USA ethical committees are commonplace in hospitals, where there is often a resident ethicist on the staff to handle the ethical aspects of clinical cases, developing policies, and education. In the UK ethical committees have been largely restricted to looking at research protocols, but the development of clinical ethical committees to act as a focus for and resource for managing difficult clinical dilemmas is accelerating.

Several of these chapters contain helpful clinical case histories, but the next edition of the book should contain another chapter, written by a clinical ethicist, with a collection of clinical cases and scenarios based on those discussed by ethical committees, together with a discussion of some of the key and contentious debate that they raised. This would demonstrate this powerful teaching method and would provide some relevant practical material for teams and trusts that are trying to set up their own ethical committees.

P Kaye

Medical Ethics, 3rd edition


Medical Ethics, to quote the authors, is intended as a practical introduction to the ethical questions doctors and other health professionals meet. The book is divided into three main sections, Foundations, Clinical ethics and Medicine and society; each section is further subdivided into topics dealt with in a single chapter.

The first section deals very well with the more contemporary philosophy rather than does not lay too much stress on the well established “four principles” (chs 1 and 2). I have rarely read such a seamless introduction to the underlying principles of medical ethics and the book’s approach would do well to be read. Later chapters deal with diverse cultures (ch 3) the human body (ch 4). Of particular note here is the excellent treatment given to information, consent, confidentiality, and truth telling. There is much to be gained here by the book’s intended audience. The chapter on the human body seems unusual in a book of this type, but is a well argued discussion of how the human body, both alive and dead, should be treated. This chapter also deals with some of the issues of post-mortem examinations and biopsies both of which are in the public mind at present; this discussion is clear and full of “common sense” and is something that should be taught to all medical students.

The general format of the chapters is to briefly discuss the medical problems and then to introduce the ethical dimension. This ensures that a reader not familiar with a certain topic is reminded of the problems before entering into the ethical discussion. The chapters on genetics and ending human lives are particularly good in this respect. Two topics not commonly found in introductory texts are included in this section, namely, psychiatry and the problems with aging and dementia. Both are discussed sensitively and with compassion and are welcome inclusions in a text of this type.

The last section contains chapters on research ethics, justice, law and “trying new things”. This rather broad area is dealt with excellently and the rather oddly named chapter on “Trying new and unusual things” is highly recommended reading for anyone wishing to introduce new treatments (medical or surgical).

Overall, the book is well organised and, while it is an introductory text, there are ample references to sustain the authors’ arguments and for further reading. Case studies are more accessible. There is a comprehensive index and bibliography. If I have a criticism, it is that the book could have been longer. However, for those who want a basic text to introduce them to life and death issues in bioethics, this is a most welcome contribution.

J Laing

www.jmedethics.com
The Use of Human Biobanks. Ethical, Social, Economical, and Legal Aspects


This booklet (freely accessible online at http://www.bioethics.uu.se/biobanks-report.html) documents a conference organised by a Swedish research project on the various social and ethical issues raised by the use of so called biobanks—that is, large collections of human tissue samples. There is considerable interest among researchers, the biotech industry, and society at large in using biobanks for the continued investigation of genetic health factors that is now following the completed mapping of the human genome. Central issues are: the responsibility of biobanks or users of these to protect tissue donors in various ways; how these responsibilities should be balanced against business and research interests, as well as against the interests of people and society in general in case of conflict and, not least, what procedures of informed consent (including the hard question of the scope of the consent) should be deemed as appropriate in the biobank setting. Although formulating these issues against the background of the actual scientific, legal, and business situation in this area, the booklet provides few answers, but outlines various studies that are to be undertaken. Because the contributions focus almost exclusively on the Swedish context (an addition of “in Sweden” to the title would not have been misplaced), this makes the relevance of this publication to a broader international audience somewhat limited. In some cases, this focus becomes so overwhelming that Swedish research ethical practice and legislation is taken for granted, without any attention being paid to differences that exist elsewhere, for example in the United States. This, as far as I am aware, is the first time such a systematic and comprehensive resource that is likely to be of value to a wide range of academic users for many years to come. It is particularly useful as a starting point for background research for bioethicists writing about topics in genetics and biotechnology. The collection takes a broad view of the different issues that have emerged from core topics such as genetic enhancement and the ethics of genetics research, to a series of sections that take the form of national reports on the political, ethical, and regulatory contexts covering genetically modified organisms. One potential problem for any reference work of this kind is getting out of date, given the changing nature of biotechnological research. The articles in the encyclopedia that we read were well written and clear, and in the main looked likely to be relevant for a while to come.

The first thing that strikes you about the two volumes of this encyclopedia is that they are very well made, attractive, solidly bound books. This impression is reinforced by first use of the word “encyclopedia.” A great deal of care has gone into making this reference work accessible and a pleasure to use. Two very minor additions that would have improved this case of use would have been to add page numbers to the list of headings and a contents page to the second volume. Nevertheless as a whole the collection was extremely easy to navigate.

The second is that we reviewed all start with a summary of the points to be discussed and then proceed to a general overview of the technology or history of the topic. For those topics on very contentious issue there is a discussion of the major arguments for and against. The headings generally have good references to other sources that will be useful for those wanting to know more.

There are very large volumes so we have based this review on a selection of its headings. Some of them are very good indeed. Dan Brock’s heading, “Cloning, ethics” is also a fascinating essay. Similarly positive things can be said about Robert Nelson’s heading “Gene therapy, ethics, germ cell gene transfer.” The section by George Wiesner, Susan Lewis, and Jennifer Scharff on “Informed subjects research, ethics and pedigree studies” was also excellent and well informed—both from a clinical point of view and also from a bioethics perspective. David Wasserman’s heading on “Behavioural genetics” is also a fascinating essay. The discussion of research into the XYY karyotype and the MAO mutation provide an excellent background to the section. Again, this section would be of interest for people wanting to do further work on his topic.

Overall, the editors have assembled an impressive cast, with many of the American names that you would expect to be involved in such a project. This does bring us to our first minor grumble: there are about a hundred contributors to this volume but only three are from the United Kingdom. This absence cannot be due to a lack of UK expertise and it is slightly disappointing that there is no contribution from writers based in the UK such as Ruth Chadwick, John Harris, or Soren Holm. This does raise the question of how attractive this volume is likely to be to the readers who are no in North America. In addition to the majority of authors, being from the USA, there is much of the public policy and legal discussion in the volumes is US centred. It is hard to see how this could have been avoided, given the authors, however, it does mean that the researcher using this text will need to be careful to ensure that he or she is used supplied of primary texts covering the rest of the world.

Given that these two volumes cost £370 it’s unlikely that any but the most enthusiastic and wealthy individual will be able to buy the encyclopedia. This is primarily a collection for libraries.

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The Human Embryo Research Debates: Bioethics in the Vortex of Controversy


United States ethicist Ronald M Green approaches the issue of embryo research (ER) in the very accessible form of a “philosophical memoir” (xv). Reporting in detail from his experience of serving on several high level ethics advisory boards, focusing mostly on his membership of the National Institutes of Health’s (NIH) 1994 embryo research panel, Green portrays both the very accessible form of these debates and the increasingly more influential form of institutionalised ethics, as well as the social and political dynamics governing its (in)effectiveness. The author also covers extensive ground regarding the subject matter of ER
itself and familiarises the reader with the technical issues and conceptual conundrums (potentiality, moral status, harming future persons) involved.

Green states in the title of _The Human Embryo Research Debate: Bioethics in the Vortex of Complexity_, that he is concerned with a plurality of debates. Examining the discourse in the US, he first deals with the different areas in which ER is debated: of the book’s eight chapters, chapters one and four stress the relevance of ER for the fields of in vitro fertilisation (IVF) research, the study of birth defects, and the development of contraceptive methods. Chapter 6 deals with the relation of ER to reproductive cloning. Green formulates a comprehensive criticism of the National Bioethics Advisory Commission’s (NBAC) 1997 report on cloning, claiming that it contributed significantly to the neglect of ER in US public policy. Chapter seven covers NBAC’s 1999 report on stem cell research, stresses the importance of ER on the form of so-called “therapeutic cloning”, and again takes a critical stance towards NBAC’s shaping of the discourse.

As the above issues are of relevance to groups with radically differing interests, throughout the book Green also deals with a second level of ER debates. This concerns the complex interplay of the interests of scientists, patient groups, the medical industry, policy makers, politicians, legal professionals, ethicists, theologians, and religious pressure groups. The dramatic clash of interests of the involved parties, the author is centrally interested in the strength of Green’s book is that it presents a transparent and valuable case study of this process. Questions regarding, for example, the criteria for selecting a competent and representative panel; how much power these institutions should be granted; what kind of standards and methodology for published reports is necessary; what degree of public participation is desirable, and how to deal with minority views, have obviously not been settled once and for all with Green’s book, but it is a stimulating and clear account which shows that these issues are just as important, difficult, and necessary as thorough academic debates on—for example, the relation of facts to values. The book will be of interest to anyone who is interested in the mechanics determining the interaction of bioethics and the political sphere; it requires no previous familiarity with the topic and can thus also be recommended to the general reader.

H Schmidt

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**NOTICES**

**The Androgen Insensitivity Syndrome Support Group (AISSG)**

The Androgen Insensitivity Syndrome Support Group (AISSG) [http://www.medhelp.org/www/ais](http://www.medhelp.org/www/ais) is a consortium of worldwide support groups, originating in the UK, providing information and support to adults and families affected by some conditions affecting the development of the reproductive system. These are conditions that have been subject to considerable secrecy and paternalism in the past, and AISSG promotes full disclosure of diagnostic information with accompanying psychological support. It also encourages recent moves to evaluate the efficacy of genital reconstruction surgery and supports the notion of autonomy and informed consent.

The conditions supported included AIS— androgen insensitivity syndrome (old name testicular feminisation syndrome or testicular feminisation syndrome)—and similar conditions, for example, XY gonadal dysgenesis (Swyer’s syndrome), 5-alpha reductase deficiency, leydig cell hypoplasia, Mayer Rokitansky Kuster Hauser (MRKH) syndrome, Mullerian dysgenesis/aplasia, and vaginal atresia.

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**9th Conference of the ABA: “Virtue and Vice in Bioethics”**

You are invited to the 9th Conference of the ABA: “Virtue and Vice in Bioethics” on the 3–6 July 2003. The venue is Queenstown, New Zealand. Confirmed invited speakers: Art Frank, Carl Elliot, and Annette Baier. Further information: Pat Johnston, Dunedin Conference Management Services, New Zealand (tel: +64 3 477 1377; fax: +64 3 477 2720; email: pat@dcms.co.nz).