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 parents desire to PGD for “milder” conditions and adult onset conditions for which they are not comfortable to have traditional prenatal diagnosis and termination of pregnancy.

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 offered PGD for Huntington’s disease 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 utilising 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 the case where the length of time it would take 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 concern for the child of having a mother suffer from early onset Alzheimer’s disease is 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 age of onset of the Val171Leu 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 (isoleucine 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 using 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 being susceptible to any genetic disorder, 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 suicide has attracted 125 responses at the time of writing. An important feature of electronic correspondence is that any peer review process would deal with any written response to them. 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 at 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 sufficiently 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”. 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.

As an editor, I feel as if I am caught in the maelstrom of the web. 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 articles which contribute to knowledge. But should be the publication of scholarly JME paper version of the journal.

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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 the most obvious starting point: the ethical discussion. The chapters on genetics, the human body, both alive and dead, should be read by anyone who expects a textual discussion of the ethical dimension. This ensures that a helpful contribution is intended to set up their own ethical committees. Finally, there is often a resident ethicist on the staff to help with difficult 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 forum 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 difficult debate that they raised. This would demonstrate this powerful teaching method and would also 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 divided 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 would do well to read this. Chapter 10 in particular is a most welcome contribution. 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 encourages the ethics of postmortem examinations and biopsies both of which are in the public mind at present; this discussion is clear and full of “common sense” answers to what is sometimes a very difficult question. The discussion of the ethical problems of mixed cultures is an unexpected inclusion and there is reliance on more contemporary philosophy rather than traditional arguments. The New Zealand background of the original edition shows through most obviously in this chapter but this does not detract from the arguments put forward.

The “meat” of the book, however, is in the second section (142 pages out of a total of 297). The “standard” topics of genetics, prenatal problems, birth, organ transplantation, AIDS, euthanasia, and brain death are all dealt with well and clearly, especially transplantation. 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 familiar with a 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 dealt with 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 final section covers 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 used extensively throughout the text to illustrate the discussions. In my opinion, the authors have succeeded in producing a text that is a practical introduction to medical ethics. I would warmly recommend this book to all medical and nursing students and a copy should be in all medical libraries.

T Russell

Encyclopedia of Ethical, Legal and Policy Issues in Biotechnology


This encyclopedia is an important 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 by bioethicists writing about topics in genetics and biotechnology. The collection takes a broad view of the field, ranging 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 informed, 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 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 increased this ease 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.

I have 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 issues 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.

These are very large volumes so we have based this review on a selection of its headings. Some of them are very good indeed. Dan Broek’s heading, “Cloning, ethics,” is the ideal introduction to the topic and one that would be useful as a required reading. Similarly positive things can be said about Robert Nelson’s heading “Gene therapy, ethics, germ cell gene transfer.” The section by Georgia Wiesner, Susan Lewis, and Jennifer Liss on “Human genetic enhancement, preimplantation diagnosis, and the human embryo” is 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 XY XXY karyotype and the MAO mutation provide an excellent background to the section. Again, this section would allow a reader interested in the issue of the origin of sex to use the encyclopedia. I would also like to see a number of other sections that are included in the encyclopedia. For example, there are no sections on the ethics of gene therapy, the ethics of the use of human tissue samples, or the ethics of consent. The sections on research into the XYY karyotype and the MAO mutation provide an excellent background to the section. Again, this section would allow a reader interested in the issue of the origin of sex to use the encyclopedia. I would also like to see a number of other sections that are included in the encyclopedia. For example, there are no sections on the ethics of gene therapy, the ethics of the use of human tissue samples, or the ethics of consent.

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 not in North America. In addition to the majority of authors, being from the USA, 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 they are used sufficiently. In summary, this is an excellent resource for those wanting to know more.

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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 project 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 biobanking 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 in Sweden and other parts of the West. For example, Mats G Hansson states, as a basic feature of the ethical background to biobank issues, that it would be disrespectful of researchers’ integrity if their control over collected research materials, data, and results were limited by regulation; and he claims that this can be inferred from the traditional legal right of Swedish individuals to have such control. This presupposes, however, that this tradition (which is hardly a given from an international perspective, where universities and funding parties are often granted much more control) should be taken as universal—a presupposition that clearly begs relevant ethical questions. The value of the booklet is further impeded by the lack of a substantial overview chapter (either at the beginning or at the end) which could have served to tie together the rather heterogeneously written pieces on the ethical, legal, and institutional strategies and research ethical conflicts; empirical as well as normative studies of informed consent, and issues of civil as well as public law into a coherent picture of the biobank issue. These chapters of most interest from an ethical point of view deal with the basic conflict between individual integrity and social utility (Mats G Hansson); what model of informed consent is most appropriate in a biobanking setting (Stefan Eriksson), and uncovering cultural conceptions of the body and its parts (Jacob Dahl Rendtorff). The treatment of these areas is rather shallow, however, in several respects. For example, although the fact that a biobank may be used for different purposes (apart from basic research, diagnosis, treatment, and securing quality of care) is noted by Hansson and Eriksson; no attempt is made to investigate to what extent different considerations are given different conclusions may be more or less applicable depending on what use of biobanks is being considered. Another example is Eriksson’s somewhat long-winded account of various “models” of informed consent, which does not serve to clarify any of the underlying normative issues, such as the question of what ultimate value such a model should be taken to serve or what is more precisely meant by the notion of an “autonomous” consent. In spite of this, however, Eriksson makes several bold normative statements in the form of three principles (of which two seem to be mere logical consequences of the first one)—though, Unfortunately, without any hint of supporting arguments. Hansson’s idea of two principles of integrity (one about the individual’s right to control biobanks because of his right to influence the policy making process) is equally lacking in underlying reflection, since he fails to note that controlling what happens to me or parts of my body may very well mean that I cannot delegate some such decision to someone else.

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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” (xxv). 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 embryonic stem cell panel, Green portrays both the intellectual obstacles and this 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 Debates: 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 complexity of the interests of scientists, patient groups, the medical industry, policy makers, politicians, legal professionals, ethicists, theologians, and religious groups with radically differing interests, for example, XY gonadal dysgenesis—testicular feminization 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.

In the age of the "globalisation of ethics" it requires no previous familiarity with the topic and can thus also be applicable in the context of wrongful life cases (pages 126–128).

In the age of the "globalisation of ethics" (John Harris) in which ethics committees and advisory boards are more and more setting the agenda in bioethical policy making, the strength of Green's book is that it presents a transparent and valuable case study of this practice. Questions regarding, for example, the criteria for selecting a competent and representative panel; how much power these institutions should be granted; what kind of 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 biology and the political sphere; it requires no previous familiarity with the topic and can thus also be recommended to the general reader.