Appendix

Sample Letter to Parents

A Sample Letter to Parents for a course on Science and Society is provided.

Topics List for Bioethics

A Topics List for Bioethics provides ideas for how bioethical issues might be addressed within the context of a Biology course.

Sample Case Study

The **Case Study: Pennington's Sweetie Pie** involves issues related to organ transplantation using genetically modified animals as donors. It is included as an example of ethical analysis and classroom application. In this section, the Case Study itself, as well as **Classroom Teaching Example**, are provided. A more detailed **Ethical Analysis** of the case follows. Lastly, **General Background Information** on genetically modified organisms is included.

Additional Case Studies

Three additional sample cases are provided:

Two Tales of Rice focuses on questions surrounding genetic modification of food.

Talk About Short explores the use of Human Growth Hormone for short stature.

One Family's Dilemma looks at the choices a family must make about their frozen IVF embryos.

These can be used in conjunction with some of the strategies provided in the primer (see the Case Study and Decision-Making Model sections).

Recommended Resources

Recommended **Online Bioethics Resources** are provided. These include curriculum units, teaching resources, films, and further reading.

References

References cited in the Primer text are noted.

Model Letter to Parents

To: Parents/ Guardians of _____

Subject: Science and Society

Your student is enrolled in the course _____.
As part of this course, we will be learning about issues related to science and society, and discussing them in class. I am very excited about the course, the issues to be discussed, and our class format. Most importantly, I am very pleased to have the opportunity to teach and exchange dialogue with your sons and daughters in our academic setting. This class will be discussing some very controversial issues and that has served as the primary initiative behind this letter.

This course will investigate the dilemmas that science and technology have created in modern society. Students will be expected to investigate and actively problem-solve selected issues that are currently being debated by scientists, politicians, and philosophers. Upon completion of this course, students will have a heightened awareness of the impact that scientific discoveries have on society.

Students will be expected to present their ideas in a structured and analytical way, and this course will strive to introduce philosophical reasoning into their intellectual growth. We will not advocate any one position in the issues we address – rather, we will try to investigate the perspectives of many different stakeholders. By learning about different ethical perspectives, points of view, and decision-making models, students will have tools to approach controversial issues systematically and thoughtfully, and be better-equipped to be effective citizens in our democratic society. We will respect and honor the family and cultural values that students bring to our discussions at all times.

Enclosed you will find the course syllabus, which lists the topics that will serve as the focus for class debate, discussion, and research. Some students may, with prior permission, elect to research topics not on the syllabus.

We will be using the following text: (list text if appropriate, and indicate whether the text has been approved by the district's Instructional Materials Committee). We will also be using materials for class discussion from various sources including newspapers, periodicals, professional medical journals and several bioethics publications. I will supplement the issues with films that are related to the topics being discussed. Should you wish to review the reference materials, I will have them available in my classroom. Feel free to call and come by to visit.

I am personally committed to making this class a meaningful one that will provide your student with the thinking skills necessary to resolve some of these issues as they confront them in their personal lives. I am looking forward to an exciting semester, and your student is what will make it all worthwhile. Thank you for the opportunity to be a teacher for them.

Based on a letter provided by William Monahan, Eastlake High School, Lake Washington School District, Washington.

Topics List for Bioethics

Cells
- Use of stem cells
- Use of patient cells for cell lines (who owns the cells and discoveries made with them?)

Characteristics of Life/Death
- Termination of care for anencephalic infants
- Definitions of death in relation to terminating life
- Assisted suicide for the terminally ill
- Artificially sustaining and prolonging life

Environmental Ethics
- Fair allocation/use of resources
- Intrinsic value of species

Genetics
- Privacy of genetic information
- Ownership of genetic information (patenting)
- Genetic modification of bacteria, plants, animals, or humans
- Genetic modification of food
- Gene therapy
- Genetic testing issues
- Personal responsibility and genetic determinism (how much is your behavior due to your genes?)

Human Biology/Organ Systems
- Use of growth hormone (therapy vs. enhancement)
- Use of steroids
- Xenotransplantation (transplantation of animal parts to humans)
- Organ transplantation
- Combining humans and computers (what makes us human?)

Microbiology
- Compulsory vaccination
- Quarantine for infectious individuals

Reproduction
- Eugenics
- Use of Pre-Implantation Genetic Diagnosis, either to select for or against certain traits
- Reproductive cloning of humans
- Cloning of animals and plants
- Sex selection
- Having one child to save another

Research Ethics
- Use of humans for clinical trials (testing new treatments, devices, or drugs)
- Human testing in vulnerable populations or in less developed countries
- Use of animals in medical research, dissection, or in testing of personal care products
- Appropriate use of genetic material sampled from indigenous populations

Other
- Health care justice
- Drugs, children, and behavior control
- Race (definition, value, use of genetic difference in medical treatment)
- Gender (definition, value)

Pennington's Sweetie Pie

Robert Pennington was a normal healthy seventeen-year-old working in a family-owned carpet store when he came down with what he thought was the flu. After a few weeks, he was not feeling better, and in fact, he felt much sicker. A glance in a bathroom mirror revealed that the whites of his eyes had turned yellow.

Alarmed, Robert went to a local medical clinic where the physician saw him. The doctor examined Robert and asked for a urine sample. Astounded by the coffee-colored brown urine sample, the doctor referred Robert to a specialist. Four days later, Robert was admitted to Baylor University Medical Center diagnosed with sudden and overwhelming liver failure.

Dr. Marlon Levy, a transplant surgeon at Baylor, knew that Robert would die in a few days without a liver transplant and reacted immediately by placing Robert at the top of the transplant list. However time was critical since Robert was showing signs of acute ammonia poisoning as a result of the liver's inability to clean toxins from his blood. He was already hallucinating and approaching a comatose state. Dr. Levy soon realized that no human liver would be available in time to save Robert's life.

Dr. Levy began to evaluate another possibility. An experimental procedure known as extracorporeal perfusion using a transgenic pig liver had been approved by the FDA for testing at Baylor Medical Center. This research was funded by a company that had developed a process to insert human genes into pig liver cells to prevent humans from rejecting a transplanted pig liver. The company then sought research hospitals willing to test the transgenic pig livers on humans with liver failure who needed a new organ. The data collected and the outcomes of these experimental surgeries, if positive, would be submitted to the FDA to support a marketing application.

The company had shipped the transgenic animals to the Baylor animal labs and they were there at the time that Robert Pennington was admitted to the hospital. Dr. Levy had also been trained in the use of these pig livers in extracorporeal perfusion. This procedure involves removing the patient's blood through plastic tubing and cleansing it by passing it through the pig liver before returning the blood to the patient. This is a temporary measure referred to as a "bridge to transplant", and it is intended to support liver function and the patient's life until a suitable human liver can be found.

Within a short time, Robert lapsed into coma and was placed on life support. Dr. Levy notified Robert's grandmother, his guardian, that she was needed in the intensive care unit for a discussion on Robert's condition. Charlotte Pennington listened as Dr. Levy explained the procedure. He also explained that, since the procedure was new, there were unknown risks that included the possibility that some dangerous animal viruses might infect Robert. He would need to be tested for animal source infections possibly for the rest of his life. Dr. Levy also told Mrs. Pennington that Robert would be his first pig liver transplant patient. Mrs. Pennington gave her consent the next morning.

Dr. Levy then removed the liver from a 15-week-old, 118-pound transgenic pig from the Baylor animal lab and moved it to Robert's bedside to be used as Robert's external support liver. Shortly after the liver was attached to Robert through the plastic tubing, perfusion began and was used for six and half hours over three days. At that point, a suitable human liver for Robert was found in Houston and delivered to Baylor for transplant. The transplant was successful and Robert made a full recovery. However, no one could forget that his survival was due to the experimental procedure Dr. Levy used to keep Robert alive until the human liver was found. In fact, Robert's grandmother keeps a snapshot of the pig, named Sweetie Pie by one of Baylor's animal handlers, in a scrapbook.

Sailing into uncharted waters, Pennington (with his grandmother) was the first subject of an experimental procedure in which his blood was circulated through a pig's liver outside his body. While all went well with Robert Pennington (and another 5 patients who received the same experimental surgery), the FDA shut down the perfusion trial three weeks after Robert's procedure. A group of virologists in England had found evidence that human cells could be infected with pig viruses* in test tubes and that the genes for two separate viral strains had been found in several varieties of pigs, making it unlikely that pigs could be bred to remove the virus.

No one knew at the time whether pig viruses could make humans sick but precaution seemed justified. Ultimately, the FDA lifted the ban when companies producing transgenic pigs developed a pig viruses detection test for both pigs and patients. Yet, this test alone did not resolve concerns about the infectious risk. The fact that pig viruses had been undetectable with any test for many years led researchers to suspect that pig tissues could harbor other unknown infectious agents.

**porcine endogenous retroviruses*

This case is derived from: Stolberg, S.G., Could this pig save your life? New York Times, October 3, 1999.

Classroom Teaching Example

This section describes how the Pennington Case might be used in a classroom incorporating elements of the Lesson Strategies included in this Ethics Primer.

This example focuses particularly on the use of a Decision-Making Framework, as well as a Case Study approach.

Decision-Making Framework Elements

1. Ethical Question: Identify the ethical problems confronted by the actors in the case. What has to be decided?
   - Should animals be used in research to provide "bridge organs"?
   - How do we treat patients ethically in end stage of their disease?
   - How should we balance the potential benefits of genetic engineering with the possible risks to public safety?
2. Relevant Facts: Assess the factual information available to the decision makers.
   - How are the animals cared for in lab facilities or any research facilities?
   - Who monitors research facilities that house animals?
   - What is the therapeutic worth of using pig livers as bridge transplants as opposed to mechanical devices? When should the use of a bridge organ be proposed for a patient (i.e., at what stage of their disease)?
3. Stakeholders and Values: Identify the "stakeholders" in the decisions and their concerns/values.

   Who has a stake in this decision?
   - Patients and families
   - Doctors, researchers, and the surgical team
   - Animal caretakers
   - Donor animals
   - Insurance companies
   - Biotech companies
   - FDA
   - Patients that may benefit from further animal research

In what ways might each stakeholder be affected?

- Human patients must consider their life, health and the well being of their families (financial and emotional burdens)
- Families and friends of the patients will be invested in the well being of the patient.
- Doctors, researchers and surgical teams will be affected by knowledge gained, prestige of success and their own satisfaction in providing patients with life saving measures.
- Animal caretakers may or may not be distressed by the use of the animals in this research study.
- The lives and well being of animals raised to human purpose should be considered.
- The health care system and society in general may be asked to share a financial burden.
- Society in general may be put at risk for undetected viruses or other infectious agents.
- The research company has business interests in the success of the therapy.
- Stockholders in the research company stand to gain with successful therapies; stand to lose with catastrophic therapies.
- Regulators must develop guidelines to govern the research and implementation of these therapies.
- Transgenic organs will reduce the waiting time for patients in organ failure.

Identify the values at stake in the decision

- Promotion of human and animal well being
- Protection from risk – the avoidance of harm or injury to others (non-maleficence)
- Compassion – sympathetic and caring response to others
- Fairness – a procedure for decision making that respects the concerns of all involved
- Justice – the distribution of harms and benefits
- Risk perception – assessing the likelihood and severity of potential harms
- Pursuit of scientific inquiry (integrity in scientific inquiry)
- Relief of animal and human suffering from disease through research development
- Protection of the innocent
- Economic profits

4. Possible Solutions: Identify the options available to the decision makers
    - With FDA approval, research with "bridge transplants" could be allowed in limited circumstances to provide patients in end-stage disease a chance of survival until a suitable human organ is found. This would also provide the researchers with more data.
    - Continue other research with transgenic animals that may have therapeutic benefits in Parkinson's and diabetes, but discontinue use of transgenic animals as "bridge transplants".
    - Perfect mechanical liver perfusion for patients in end-stage disease.
    - Place patients on transplant waiting lists in the hope of receiving a suitable organ. Advocate for social change in increasing the number of available donor organs through educational programs.

Case Study Approach

Have students form groups based on the 4-6 stakeholder groups identified as most important to this case. For example, students could be grouped into researchers, doctors, veterinarians, animal activists, patients and families, insurance companies, etc.

Have each group derive the concerns and values that are most important to them. If time permits, have each group conduct research on their stakeholder. If time is limited, provide each group with a 'position sheet.'

Create mixed groups consisting of students from each individual group. Have students present the position of their stakeholder to the mixed group. Allow the groups time to come to consensus on an ethical issue related to the case, or ask them to clarify the nature of their disagreement.

Afterwards, allow individual students to present their own position through a debrief session or through a written assignment.

Extension Activities:

Anatomy and Physiology:

Have students research the anatomy and physiology of the liver. This should include the normal development, structure, and function of the liver. Review the tests used to determine normal liver function and disease state. Encourage students to consider the quality of life issues surrounding someone in organ failure. Have the students link the symptoms of Robert Pennington to the physiology that they have learned.

Transplant Information:

Have students access the United Organ Sharing Network for information on:

- The number of people currently waiting for transplants
- The number of transplants that occur annually and the organ type
- The number of medical centers performing transplant surgery
- The cost of a liver transplant and the necessary follow up care
- The tissue match criteria for a successful liver transplant
- The types of tissue and solid organ transplants

Ethical Analysis of the Case: Pennington's Sweetie Pie

Robert Pennington's case exemplifies both the promise and potential peril associated with the introduction of genetically modified therapeutic animal tissues into humans. The creation of bioengineered animals as a source of tissue to treat human disease is a rapidly progressing phenomenon that has raised several practical, scientific, medical, regulatory, ethical, and social policy concerns.

Practical problems include the access to an appropriate source and number of suitable animals. Scientific concerns include the ability to adequately and reproducibly "humanize" animals with genetic alterations that effectively prevent tissue rejections in human recipients. Medical problems include the potential that these animals are a source of undetectable zoonotic infections that can infect the human recipients with symptoms arising sometimes years after transplantation during which time the patient may pass the infection to others. Other medical problems include the unknown longevity of animal organs, the degree to which they can eliminate severe organ failure, and the inability to predict the risks (both immediate and long term) of the transplant procedure. Since the field of xenotransplantation is advancing at such a fast rate, regulatory systems such as the FDA often lag behind the technology development, resulting in inconsistent and spotty controls and guidelines. Also, since corporate scientists many times hold the expertise in the field, FDA learning often comes from the companies the FDA is authorized to regulate. The combination of the promise of the technology and the related concerns (1) has generated multiple ethical and social policy issues and concerns that this teaching module is designed to address.

The ethical and social issues linked to xenotransplantation to date include:

Use of Animals

The protest of animal rights activists is exemplified by the statement of one such group: "Should xenotransplantation ever become a reality, pigs will be turned into spare part factories, plundered for their organs. Genetically-mutated and raised in artificial conditions, these remarkably intelligent animals face an unnatural and distressing existence." (2) The questions that flow from a concern about animal welfare include:

- What acuity of human need justifies the use of animals to obtain therapeutic tissue and organs?
- Are the numbers of animals used in the process of developing the technology justified?
- Is the process of retrieving tissues and organs humane?
- How do we balance the need to save human lives and improve human health with the need to respect the lives of animals?

Human research integrity

In order to justify the introduction of xenotransplantation into humans, research must be able to demonstrate that the benefits to the patient of the experimental treatment outweigh the risks. This is a difficult task, many argue, since too much is unknown about the consequences of xenotransplantation. Yet, others argue that lab and animal research are never sufficient to be able to predict human risks and benefits with any degree of reasonable surety.

A second important consideration relates to the integrity of human subject consent.

Since the patients on an organ transplant waiting list are often close to death and therefore desperate, can they rationally weigh and balance the information about the consequences of animal organ transplantation to provide free and full and valid consent? How do researchers responsibly balance the need for informed consent, take into account the vulnerability of the potential human subjects, and still pursue this potentially valuable research.

Timing of deployment

The great medical need for organs and the absence of viable therapeutic alternatives drives this technology development. The fact that patients with failing organs will often die before a suitable human organ is available tempts physicians to deploy the technology to save a life despite the lack of full understanding about the consequences of the transplant. Some ethicists believe that patient need and the lack of other options makes it ethically defensible to proceed with research despite the unknowns(3). The drive to introduce transgenic xenotransplantation in humans has been lauded by some who view these physicians as heroes willing to take risks on behalf of the preservation of human life. Others criticize scientists and doctors who push the envelope and suspect that their pursuit of personal glory drives them more than does a concern for patient welfare. These differing views often influence the speed with which new medical technologies are deployed in humans. And when they are deployed, there is always a question about whether more research is needed to ensure patient benefit. This question was addressed by one ethicist who wrote that "There is a widespread misperception that medical treatments and surgical procedures are easily classified as either experimental or accepted. In fact, all treatments have an element of experimentation, and new surgical procedures are based on extrapolations from prior work...When does a surgeon decide to apply a new operation to a patient?...the decision is based on balancing, on the one hand, the experimental evidence suggesting that the procedure may succeed, and, on the other, the clinical urgency..." (4)

Regulatory integrity

Commensurate with the ethical concerns above, commentators have asked whether the FDA has prematurely approved the use of bioengineered livers. Faith in the regulatory system can falter when, as in the case of xenotransplantation, the Agency approves of and then halts research because of the risk of harm to human subjects. In light of this public trust issue, others have asked whether the regulatory agencies should consider public as well as scientific opinion before approving human research on xenotransplantation. A European poll at the time showed that only 36% of people found xenotransplantation acceptable. In another poll, those in Britain were only 21% in favor. Others take a different approach and favor proceeding with the research but only under careful controls. The problem with this approach is that consensus on the definitions of transplant success and what constitutes adequate control and surveillance is not widespread and is likely to change as information advances.

Patient welfare

Concern for patient welfare prompts several questions:

- How many liver failure patients can be sacrificed in the process of researching the efficacy and safety of animal tissue transplantation in humans?
- How much should be known about the risks (including that of zoonoses) before the deployment of bioengineered pig tissues into humans with organ failure?
- What constitutes a reasonable balance of risks and benefits from animal organ transplantation?

Obviously, differences of opinion exist with respect to each of these questions.

Some argue that any survival benefit is justified in patients facing imminent death and any delay in the research will only lead to more deaths from organ failure.

Critics argue that we should not proceed in the face of unknown and potentially dangerous adverse consequences since we are "literally, interfering with something we do not understand." (5)

Public safety

Retroviruses such as PERV (Porcine Endogenous Retroviruses) and HIV (Human Immunodeficiency Virus) integrate into the DNA of the cells that they infect, allowing them to persist in the infected individual or animal indefinitely. Also, animals can pass infectious agents to humans, such as the prion that causes Bovine Spongiform Encephalopathy (BSE or "mad cow disease") in cattle and variant CJD in humans. The prospect of confronting infectious agents like these in xenotransplant patients (zoonotic infection) who might infect others worries some scientists, public health officials, and regulators.

As one alarmed researcher put it, "The individual can sign a consent form and say, 'I'll take the risk because I'm going to die anyway.' But that person is signing a consent form for the whole population, the whole human race." (6) To prevent such contamination, the United Kingdom agency charged with producing guidelines for xenotransplantation advised that recipients of animal organs be required to sign a document of consent agreeing to be perpetually monitored for signs of infection, to take drugs for the rest of their lives to maintain their health, to use barrier contraception constantly, to have their sexual partners consistently monitored, and to refrain from pregnancy or fathering a child.

Commercialization conflicts of interest

Any time that companies sponsor research on products intended for a lucrative market, conflicts of interest concerns arise. This is especially the case when a small biotechnology company is relying on its first product to sustain corporate viability. This situation prompts questions about whether the promise of profits prompts companies to engineer the clinical trial protocols to enhance the probability of good outcomes or to push the technology into human trials prematurely. The concern about conflicts is heightened in situations where the regulatory agencies must rely on corporate scientists to become sufficiently informed about the technology to promulgate regulatory guidelines.

Distributive justice and the cost of medical care

In 1996, the Institute of Medicine calculated that if animal organs made it possible to offer a transplant to everyone in the United States who needed one, annual medical treatment expenditures would rise to $20.3 billion, from $2.9 billion.(7) This cost estimate prompts the question of whether the potential benefit to organ failure patients is sufficient to justify the risk that constraints on medical budgets will lead to denial of medical care to patients with other diseases.

References Cited

(1) Michler, Robert. (1996) Xenotransplantation: Risks, Clinical Potential and Future Prospects. Centers for Disease Control and Prevention. EID. 2(1), January–March. (http://www.cdc.gov/ncidod/EID/vol2no1/michler.htm) accessed March 4,2005

(2) Uncaged campaigns. Xenotransplantation.(http://www.uncaged.co.uk/xeno.htm#two) accessed March 4, 2005

(3) Caplan, A.L. (1985) Ethical issues raised by research involving xenografts. J. Am. Med. Assoc. 254, 3339–43.

(4) Reemtsma, K. (1985) Clinical urgency and media scrutiny. Hastings Cent. Rep. 15, 10–11.

(5) Uncaged campaigns. Xenotransplantation.(http://www.uncaged.co.uk/xeno.htm#two.) accessed March 4, 2005.

(6) Stolberg, S.G. (1999) Could this pig save your life? New York Times, October 3.

(7) Institute of Medicine (1996) Xenotransplantation: Science, Ethics and Public Policy. National Academy Press, June. (http://www.nap.edu/catalog/5364.html) accessed March 4, 2005.

Ethical Concerns Regarding Genetic Modification of Organisms

The genetic modification of plants and non-human animals normally involves the alteration of individual traits to increase the usefulness of the organism for human purposes. Genetically modified (GM) crops may be more productive, more resilient, or more resistant to insects or disease than their natural, non-modified counterparts. Similarly, animals may have GM traits that make them more efficient sources of food or other useable products. Proposed genetic modifications in human beings involve either the alleviation of disease or disability caused by some genetic malfunction or abnormality of the individual or the attempt to enhance the phenotypic properties or functioning of the individual.

Although the genetic modification of plants and animals tends to be widely accepted in North America and Asia, it has been more controversial in Europe and in some developing countries, particularly in Africa. There are basically three sources of ethical controversy in the area of GM plants and animals.

First, some believe that ethical principles of justice, respect, dignity, the avoidance of suffering, and rights all apply to at least some species or forms of life other than human beings. According to this perspective, plants and animals should not be used instrumentally as a means to an end, but should be respected as an object of integrity in their own right. Proponents of this view argue that inherited genetic structures of individual plants and animals, or whole species, should not be deliberately altered without good reason.

The second basis of ethical concern on the topic of GM plants and animals is the potential risk to natural evolution, ecosystems, and to human health and well-being. Some feel that in the field of genetics, human scientific and technical knowledge may exceed human wisdom and prudence. Critics would say that while GM has the potential for tremendous human economic and health benefits, it has the potential for catastrophic mistakes and dangers as well.

For instance, genetic modification in agriculture tends toward genetic simplification of a population or species and undermines genetic and biological diversity. Over long periods of time, species that are genetically diverse have a greater capacity to adapt and survive in the face of changing evolutionary and environmental pressures. Genetic modification practices increase the need for human, technological support to ensure the survival of genetically simplified species, hence the increased use of insecticides and fertilizers. Over time, genetic modification may contribute to the decline of biodiversity and the disappearance (extinction) of species that is now occurring worldwide at an alarming rate. Moreover, genetically modified organisms that come into uncontrolled contact with natural organisms may spread the modified traits across an entire habitat. Genetically modified corn that was intended for use only in animal feed, for example, became accidentally mixed with corn intended for human consumption. The discovery of this

accident caused considerable economic disruption because the GM species was associated with serious allergic reactions and other health risks in some persons.

The third source of ethical controversy surrounding genetic modification in plants and animals derives not so much from the biological aspects of GM itself as from its social, economic, cultural and political implications. In areas where it has been widely developed, GM in agriculture has tended to alter patterns of family farming and landholding, giving competitive advantage of larger types of agro-business and making farmers more dependent upon the international corporations that own seed-lines and sell the kinds of pesticides and fertilizers that GM crops require. In the developing countries, genetic technologies have prompted countries to emphasize monocultural practices and to abandon crop rotation in favor of intensive fertilizer use. This has often made developing economies and the agricultural labor force in developing countries vulnerable to shifts in global commodity prices and has increased their need to import a range of foods and other products needed by their own population. When human interference with phenotypes that have slowly evolved and adapted to local ecosystemic conditions continues for some time, a danger can be posed to the sustainability of those ecosystems, and the traditional cultures and ways of life built around them.

The genetic modification of domestic animals also raises both concerns of inherent wrongdoing to the rights and welfare of the animals themselves and concerns of risks to human health. The maximization of meat, milk, or egg production has led to genetic modifications in animals that have made them unable to engage in normal repertoires of behavior and left them susceptible to various kinds of infections and disease. Farmers have responded by the widespread use of antibiotics in their herds or flocks, which raises the issue of the evolution of resistant microorganisms.

Genetic Modification in Medicine

Another important motivation for the genetic modification of animals is to make them suitable for medical research that eventually may benefit humans. Selective breeding of rat species for use in the laboratory has been practiced for many decades; quicker and more efficient recombinant methods have more recently come to the fore to produce animals selectively designed to be good models for the study of various kinds of disease. For example, mice have been genetically engineered to model a variety of human diseases including cancers and neurodegeneration.

One of the most interesting and potentially important areas of genetic modification in human medicine is in the field of xenotransplantation. This is the use of organs or tissues from one species in another species. Therapeutic xenotransplantation remains an experimental treatment, but it has a long history that flows from the first use of human organ transplantation. Early experiments with human organ transplantation eventually generated an interest in the use of animals as a source of transplantable tissue. Early experiments involved the attempt to transplant the heart of baboons into human infants; more recently pig livers have been used outside the body to sustain human liver function for short periods of time while a patient who is suffering from liver failure awaits transplant.

Aside from the sacrifice of healthy adult animals that xenotransplantation entails, ethical concerns here mainly focus on the unknown long-term risks. Genetic modification enters into this technology because normally the human body will reject an organ from a non-human source. Bioengineering of the donor animal generally involves the introduction of human genes into an animal to create tissues that are immunologically compatible with humans. These bioengineered (or transgenic) tissues are then harvested and used to replace the tissues or organs that are destroyed, diseased or failing in patients. A decisive objection to animal to human xenotransplantation at this time remains the possibility that viruses indigenous to one species may inadvertently be introduced into the human recipient. This could be very deleterious to the health of the human patient, even fatal, and might threaten others as well if the agent were to prove contagious or infectious.

Xenotransplantation Time Line

1923	First cited xenotransplant: lamb kidney was transplanted into a human who dies nine days later.
1960s	Xenotransplants involving baboon or chimpanzee kidneys.
1960	Transplant experiments with dogs begin.
1963	Dr. Thomas E. Starzl of University of Colorado, Denver, attempts the first liver transplant. The patient dies within a few days.
1964	Cross-species transplantation experiments.
1967	Barnard performs first human heart transplant (patient dies of pneumonia 18 days after transplant).
1967	Dr. Starzl performs the first successful liver transplant. The liver functions for 13 months.
1967–69	More than 100 transplants performed (65% of patients died within three months of the procedure).
1969–74	Dr. Starzl transplants chimpanzee livers into children. The survival time ranges from 1 to 14 days.
1968	Colley and Ross transplant sheep and pig hearts, respectively, into dying human recipients. Both patients died.
1984	"Baby Fae" infant with hypoplastic left heart syndrome receives a baboon heart. She dies 20 days later.
1992	Doctors at Duke University use a pig liver as a bridge to keep two women alive who were awaiting transplants. In one patient, the liver is kept outside the body and hooked to the liver arteries. She survives long enough to receive a human liver. In the other, the pig liver is implanted beside the patient's liver and she lives for 32 hours.
1992	Cazplicki reports an attempt to transplant a pig heart into a human patient using novel immunosupression therapy. The patient died 24 hours later.
1992	Makowka transplants a pig liver into a 26-year old woman dying of acute liver failure. The organ immediately failed.
1997	Robert Pennington receives a "bridge" to transplant extracorporeal pig liver.
1997	More than 250 pig farmers in Malaysia became ill with encephalitis and 101 died. Pigs were identified as the source of the virus.
1997	FDA and its U.K. counterpart call for moratorium on all xenotransplantation.
2003	FDA, NIH, CDC, and HRSA develop guidelines on xenotransplantation and clinical trials can resume.
2000's	Ten Swedish patients with diabetes receive cells from pig pancreas. The cells do not produce insulin as hoped; however, none of the patients become ill from the xenografts.

Additional Online Resources for the Pennington Case

MacDonald, L. Ethical Issues in Genetic Engineering and Transgenics (http:// www.actionbioscience.org/biotech/glenn.html) Accessed March 4, 2005.

Grey, S.T. Genetic Engineering & Xenotransplantation (http://www.actionbioscience.org/biotech/grey.html) Accessed March 4, 2005.

Moreau, J. Xenotransplantation (http://www.bioethics.upenn.edu/highschool/Briefs/?t=1&a=47) Accessed March 4, 2005.

Transgenic Mammals: "Wilbur" as another instrumental good (http://www.accessexcellence.org/AE/AEPC/WWC/1992/transgenic_mammals.html) Accessed March 4, 2005. Annotation: This site provides good resources for teachers and students separately.

Front Line (2001) Organ Farm - Part 1 (links to Part 2) Program #1912 Original Airdate: March 27, 2001 (http://www.pbs.org/wgbh/pages/frontline/shows/organfarm/four/#rp and http://www.pbs.org/wgbh/pages/frontline/shows/organfarm/etc/script1.html) Accessed March 4, 2005.

Cowely, G., Underwood, A. and Brownell, G. (2000) A Pig May Someday Save Your Life. Newsweek. January 1. (http://www.keepmedia.com/pubs/Newsweek/2000/01/01/317413?extID=10026) Accessed March 4, 2005. Annotation: Scientists are racing to turn oinkers into organ donors. The effort could bring huge benefits, but it carries huge risks.

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'Pillow Angel' Ashley X

Ashley was 6½ years old when she was diagnosed with static encephalopathy, a condition in which her brain is in a permanent and unchanging state. Ashley's parents, who also have two other healthy children, had cared for Ashley in their home since birth, as Ashley's development equaled that of an infant. Ashley could not roll over, sit up or hold her head up, or use language.

Ashley's parents grew concerned over their abilities to continue to care for Ashley at home. With her continued growth and development, she would eventually become too large for them to manage her needs, including feeding her, changing her, bathing her, and positioning her during the night. Additionally, they were concerned at the prospects of her sexual development, including menstruation, breast development, and her fertility.

Ashley's parents made three requests of doctors at Children's Hospital and Regional Medical Center in Seattle, Washington. First, they wanted Ashley to have a hysterectomy — in which her uterus is removed — to prevent any risk of menstruation and/or pregnancy. Second, they requested the removal of her breast buds, which would eliminate the development of breasts altogether. Ashley's parents argued that her breasts would cause discomfort with the straps used to hold her in her chair, and that breast discomfort was a known problem for some adult women in the family. Finally, Ashley's parents requested medical treatment to limit her final adult (known as *height attenuation)* height and weight through hormone therapy.

The ethics committee noted that there was great need for caution for such a procedure, as there have been many documented cases of past abuses of people with physical and developmental disabilities. Dr. Doug Diekema (who, with Dr. Daniel Gunther, published their paper on Ashley in the *Archives of Pediatric and Adolescent Medicine*) noted that although there were few concerns regarding the hysterectomy and removal of breast buds, there was greater concern for the hormone therapy and resulting height attenuation.

Critics noted that the use of surgery and hormones to prevent a person from maturing into an adult was unprecedented in medical history. There were also worries about Ashley's rights as a patient, as her parents were making this decision without her ability to contribute. There was a general concern for the potential 'slippery slope' of adapting the bodies of the disabled to suit the needs of the caregivers, unless it could be justified that this change was also in the patient's (Ashley's) best interests. An ethics consultation involving about 20 individuals was performed prior to making the decision. The consultation included a developmental specialist, Ashley's primary care provider, and her hormone specialist. Although Ashley's parents attended the consultation, they were not a part of the deliberation.

After a lengthy consultation with parents, family, physicians, and the Seattle Children's ethics committee, a consensus was reached to perform the full treatment. A simple hysterectomy was performed on Ashley, although her ovaries were preserved in order to allow for normal hormonal production throughout her life. Her breast buds were removed without complication, and Ashley's height attenuation treatment included an estrogen skin patch applied daily for 2½ years without complication. Estrogen is the primary female hormone that, when used in high doses, shortens the amount of time that growth can occur.

One year after her treatments, at the age of 9, Ashley was 4'5", about 12 inches shorter than predicted without therapy. It was estimated that her weight — 65 pounds — was almost half of what it would be without the hormone treatments. She continues to live under the care of her family.

To Think About

Do you think that the Review Board made the right decision about Ashley's treatment? Why or why not?

Underlying all of the ethical debates is the question of who should be able make decisions regarding the welfare of a profoundly disabled child. How much freedom should parents have to make decisions for their children, and at what point should their choices require review by someone else (like a court)?

Some people have argued that permitting this kind of medical intervention in a patient with a profound and permanent developmental disability creates a slippery slope. They fear that even if these treatments were appropriate in this one case, they might be used inappropriately in others. Is there an answer to this slippery slope argument?

Some people have argued that this brings us back to the days of eugenics. Does it?

This case was met by the expression of great concern from some members of the disabilities community. They considered themselves to have a stake in this decision as well as the parents and Ashley. Are there other stakeholders in this situation? How do each of the stakeholders stand to be harmed or benefited? How does one resolve a conflict between stakeholders? Should an ethics committee weigh the claims of all stakeholders equally?

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Contributed by Jacob Dahlke, Seattle Lutheran High School, based in part on materials by Doug Diekema, MD, Seattle Children's Hospital Research Institute

Two Tales of Rice

Rice is the major source of calories for approximately half of the people on the planet. In much of Southeast Asia, people get more than half of their total calories from rice! In China, an average person consumes over 200 pounds of rice a year (in the United States the figure is only 20 pounds a year). In many of the regions where rice is the main food staple, there is also very high childhood mortality caused by malnutrition, diarrhea, and infections resulting from compromised immune systems.

In the United States, rice may not be as common a food source as wheat, but it still occupies an important role for producers/exporters, and for those who retain its cultural value. For many Americans, the subject of rice is only important when we are ordering take-out food and are asked "steamed rice for how many?" However, rice is at the heart of much controversy throughout the world.

Consider these two different tales involving rice and genetic modification.

Golden Rice

In the early 1990's various publicly funded international scientists teamed to develop rice that would provide Vitamin A, which had been identified as one of the three main diet deficiencies in developing nations (the others were iron and iodine). The project proposed to genetically engineer genes from the pathway that creates beta-carotene in daffodils into rice endosperm. Beta-carotene is then converted by the body into Vitamin A. The process of trial and error took ten years. The potential product was called "golden rice" for its distinctive colored grains.

In 2000 the scientists announced their successful results. They had created transgenic rice plants that were capable of producing the yellow-colored endosperm that contained Vitamin A and other related compounds of nutritional value. The July 2000 issue of *Time* magazine featured the most outspoken of the creators, Dr. Ingo Potrykus, Professor Emeritus of the Swiss Federal Institute of Technology, with the headline: "This Rice Could Save a Million Kids A Year," which referred to the number of childhood deaths attributed to Vitamin A deficiency by the World Health Organization. At the time of that publication golden rice was considered a major breakthrough in biotechnology because the researchers had engineered an entire biosynthetic pathway. The scientific process for genetic engineering of rice had been a success, but the battle for acceptance was just beginning.

Golden rice has faced opposition primarily from environmental groups that are opposed to any use of biotechnology on the food supply, and view Genetically Modified Organisms (GMOs) as possibly leading to problems such as decreased biodiversity, human health and environmental risks, and the economic exploitation of subsistence farmers in developing countries. Golden rice 2 has now been developed, and provides 23 times more beta carotene than the original, but the rice is not yet available for human consumption in any part of the world.

Golden rice was developed with public funds and its creators carefully tried to keep their patent in the hands of a humanitarian organization so that its distribution could more readily serve their goal of meeting an urgent need. In the Time magazine article of 2000, golden rice was said to be "the first genetically modified crop that was inarguably beneficial." Its methodology involves transgenics, moving genes from one species of plant to another. Vitamin A deficiency (VAD) has been associated

with one million childhood deaths per year; with up to 230 million children at risk of VAD, and 500,000 cases of blindness per year. Opponents state that there are other ways to alleviate Vitamin A deficiency.

Ventria's Rice

In May 2006 a company with sixteen employees, Ventria Biosciences, announced that they were developing a drug that would be used to fight diarrhea. According to the UNICEF report, "The State of the World's Children 1998,"diarrhea ties with Acute Respiratory Infections as the cause of 18% of deaths in children under five in developing nations, worldwide. Deaths due to diarrhea are considered preventable, and it would seem that a drug to fight diarrhea would be welcome news. Instead the small company's announcement caused a furor among environmental groups, food corporations, and thousands of farmers. The reason involved their plan to grow the experimental drug in rice that had been genetically engineered by splicing human genes into the crop. The US Rice Producers Association has been particularly vocal in their criticism of Ventria's experimental work and the company had been forced to relocate from California to North Carolina, after rice customers in Japan refused to import California rice as long as Ventria was operating in that state.

The opposition to the experimental drug that is the proposed product of Ventria's genetically engineered rice stems from its use of the most controversial form of agricultural biotechnology, known as "biopharming." Biopharming involves splicing human genes into crops to produce proteins to be used for medicinal purposes. The proposed drug from Ventria would be a protein powder milled from the rice and would contain two human proteins that are commonly found in a mother's milk, saliva, and tears. This protein powder is designed to help patients hydrate and may lessen the severity of serious diarrhea attacks (3.67 days versus 5.21 days in data presented at the Pediatric Academics Societies Meeting, San Francisco, 5/06).

Ventria's proposed product involves the use of human genes spliced with those of a crop, and grown as part of a for-profit endeavor. The company hopes that the resulting protein powder could be marketed as a "medical food" rather than a pharmaceutical and has applied to the Food and Drug Administration (FDA) for approval as such. If the protein powder is considered as a pharmaceutical it will be subject to human tests, resulting in a far lengthier process for approval. Diarrhea is considered a major childhood killer in developing countries. However the protein powder, while lessening the severity of attacks, does not have any preventive properties. Opponents also point out that other preventive measures are more useful in preventing diarrhea, along with educating health care providers and caregivers on the necessity of rehydration.

The arguments against the development of golden rice and Ventria's rice are similar, with opponents stating that growing genetically engineered crops will threaten the safety of conventional crops and decrease needed biodiversity. Trade groups and producers such as Riceland Foods Inc. (the world's largest rice miller) fear that nations that completely oppose GMO's, such as Japan, will refuse to buy US crops. Exports account for 50% of the rice industry's sales. The scientists involved with each GMO rice counter that rice is "self-pollinating" therefore it is virtually impossible for genetically engineered rice to cross breed with traditional crops.

To Think About

The case describes two different projects involving genetically engineered rice. Would you support one over the other? If only one type of rice could get approval, which rice would you choose?

Do you think that genetic engineering of foods is ever justified? If so when?

Does it make any difference in your decision-making process about who stands to profit?

Does biopharming using human genes seem more threatening than genetic engineering using plant genes? Why?

Could opposition to biopharming lead to a decrease in opposition to transgenic work such as golden rice?

Should golden rice be available for human consumption in developing nations? What about in the U.S.?

Do you think the FDA should consider Ventria's product as a "medical food" or a drug? What factors would you consider in deciding?

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Case written by Peggy Sturdivant

Talk About Short

Zack knows the waiting room drill by heart. From the second the door opens he can sniff out new patients and how late the doctor is running on his appointment schedule. Pediatric Endocrinology. Zack used to wish that he'd never heard the words in his life. If he were a late night comedian there could be some very non-PC material in the waiting room. "How short were they?" the audience would shout. He could say, "The patients were so short that the fish tank was at floor level. They were so short that there were step stools so that they could climb onto the kindergarten size chairs..." But it's not really true. Short stature isn't the only metabolic disorder. Still, the waiting room always has a disproportionate number of boys, most of them still baby-faced. The first-timers usually have two parents with them. Everybody looks at one another but tries not to get caught doing so. Zack often wonders if the other patients are already taking recombinant growth hormone (rGH) or whether the family is in the early stages of trying to learn why "Johnny is so short."

Zack is aware that he's older than most of the others. He is getting dangerously close to puberty cut-off, when he may not even be a candidate for growth hormone. And at age thirteen, 4'11," what are the real chances that his own pituitary gland will kick start a growth spurt? There have been times that he wished that he were anywhere but in Dr. Bass's waiting room or at the Pediatric Clinic for tests. Zack does still wish that that he wasn't an on-line expert in growth hormone literature (diagnosis, prognosis, and ethical concerns!) and that he had never heard of "Idiopathic Short Stature". He laughs to himself when he thinks about this term. Maybe because his short stature is of unknown origin (his parents are of average height and his pituitary gland is apparently able to produce growth hormone) some people want to coin him an idiot for caring about his height when other people have "real problems."

He's the older of two boys. His younger brother Ben (he can't call him his 'little' brother any more), is four years younger. When Ben was as tall at five years old as Zack at nine, his parents seemed to freak out. First there was the family doctor for more measurements, then the referral to a specialist and since then there have been the X-rays of his left wrist, the nutrition consultations, the sleep study, and mostly, the years of blood tests. It seems kind of funny that the specialists don't have one single test to determine what they really want to know, which is whether Zack's endocrine system is working properly to signal the pituitary gland to produce growth hormone and the other hormones that control his thyroid glands, adrenal glands, and sex glands. The hormone is produced in spurts, usually during deep sleep and so doctors have to look indirectly for the byproduct (somatomatin) in his bloodstream. The tests have showed that Zack is not completely deficient in growth hormone; his body makes it, but not enough to help him grow enough to be considered "normal." There's also a possibility that he's simply a male whose growth spurt is going to occur somewhat later than the average.

Anyway, the insurance company turned down the doctor's recommendation for growth hormone treatment when he was eleven years old and four feet tall. They said that since his body was producing growth hormone, and he was not at the crucial 2.5 deviations from the norm, that the treatment was not warranted based on medical need. That was fine with Zack when he was in fifth grade. His parents had tried to sound so gung-ho like it would be fun to mix up powder and water every day and inject it into himself. A powder, that he'd overheard a hundred times in his mother's crusade, which cost $20,000 a year, up to $40,000 if it was injected every day of the week. But the average gain in height with growth hormone is only 1-2 inches. Zack can see why the insurance company thinks that $20,000 an inch is too expensive.

What's really strange is that Zack didn't ever think of himself having a problem until his parents got so concerned about his height. He had friends; sure they were each a bit taller than him but it hadn't been a big deal. No one had ever picked on him because of his height, maybe teased him about the bat being too big for him but it hadn't stopped him from hitting quite a few three-base hits.

When the specialist first confirmed that Zack's growth was not keeping up with the average it seems that his "problem" wasn't abnormal enough.

If his body wasn't producing any growth hormone then no problem, the insurance company would pay for treatments and he would be an old hand at self-injection by now. His mom had an entire stack of letters that she had exchanged with the insurance company as she waged a battle to get them to cover his treatment on the grounds that "early treatment works best" and that psychological damages would continue to mount. He tried to tell his parents that he thought he was going to have a late growth spurt, he didn't really feel "psychologically" damaged, but they were adamant that the world is very cruel for short people. They were going to battle the insurance company for his right to treatment. Zack didn't know how to feel about it; sometimes he was tempted to ask his mother, "Would you be fighting to get me growth hormone if they still had to extract it from corpses?"

Zack is sure that he and his mother are reading the same web sites, reviewing the latest articles cited on the Human Growth Foundation site and the links that he finds when he does a Google search. His mother as always seemed so sure about what they should do, but he's not as certain. When the FDA approved human growth hormone use for "short stature" in 2004, the review committee said they weren't convinced that short stature constituted a medical condition, but that the treatments didn't seem harmful. The possible side effects include headaches, bone aches, a diabetes-like condition, and potential effects later in life from having stimulated cell growth. He has read that boys are twice as likely to be referred to specialists as girls, but that once there, girls are the ones who usually have a diagnosable health problem. There's also a quote from Dr. Alan Rogol that appears on all the web sites against growth hormone therapy. The quote says, "Short stature became a disease when unlimited amounts of growth hormone became available."

Growth hormone therapy does not work overnight. Zack has read that many people think that small kids are like a seed that is ready to germinate if you add water, and Miracle-Gro. Meanwhile he has been rechecked, resized, his blood work updated, and he is getting his first injection today. After nine months of a plateau of 4'11," the insurance company has agreed to cover three injections a week for up to three years. For the first month he will receive the injections at Dr. Barr's office, to monitor and get him used to proper mixing and injection techniques. After all the years of wishing that his parents wouldn't make such a big deal he is actually excited about trying the treatments. His friends have all shot up recently and he has that sense of being smaller than everyone else. At the library, the librarians eye his friends with skateboards under their arms like they are a dangerous menace, but their smiles at him seem to be saying, "Oh, isn't he cute?" Zack knows he is never going to be tall. If all goes well he'll be at least 5'3" since he could still have a natural growth spurt. He had always thought that it wasn't that bad being different from others, but that was before he felt so different. The girls have gotten so tall. Of all the couples that have suddenly developed in eighth grade, not one of the girls is taller than the guy. Maybe his parents had always been right to fight for this; they had known before he did that he was going to want to be more normal. It's strange because after his mom won the fight with the insurance company, she told him that the decision about whether to have the therapy was up to Zack. "I just always wanted you to have the choice," she told him. "Didn't you know that?"

One day there was a really pretty girl in the waiting room; she looked about his age. But she looked at Zack like she hated him. He'd seen a lot of short kids over the years, and could usually tell by their proportional bodies or chubby faces whether their short stature or size was a result of more severe endocrine malfunction. This girl was small all over and Zack had to admit that he found himself thinking how doll-like she was, like a magazine model but in miniature. She looked at him with loathing as though assuming (correctly) that he was thinking that she just looked "so darn cute." It was one time that he wished that he were shorter so she would look at him as an ally, instead of an enemy. But after that day he started noticing when people were looking at him as though he were cute and adorable. It made him feel angry too. He used to wonder why appearance seemed to be so important at school, in movies, everywhere. Now Zack has stopped wondering; it is a reality. He lives in a culture that prefers men to be tall; and a few headaches or bone aches don't seem like much of a price to pay. He can't wait to start the therapy and make up for all the lost years.

The inner door opens and the nurse announces, "Zack, we're ready for you."

To Think About

Zack's family has health insurance and the treatments will be covered. If he was an uninsured male teenager, should he have the same right to treatment?

Do you think that Short Stature should be considered a medical condition? How would you define it?

If you were a short girl instead of a short boy, do you think it would make a difference?

What points would you make to convince Zack not to have the treatments?

What if Zack were against receiving Human Growth hormone but his parents insisted; at what age do you think a child should decide versus a parent?

If Short Stature is not considered physically dangerous, should potential psychological damages need to be proven before treatment is approved?

Should treatment criteria be different for treating an illness that is life-threatening or will be fatal in the long-term?

Pediatrician Alan D. Rogol has stated, "Short stature became a disease when unlimited amounts of growth hormone became available." Would it make a difference in considering treatment to think that the demand was due to pharmaceutical marketing instead of actual need?

If you had Idiopathic Short Stature, would you want to receive recombinant (biosynthetic) growth hormone? What if the growth hormone that was harvested from the pituitary glands of corpses was more effective and still available? Would you use it?

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Case written by Peggy Sturdivant

One Family's Dilemma

Kathleen knew that there was quite a bit of controversy regarding stem cell research in the news, but it didn't occur to her that it really affected her in any way. Then again, she had never thought the word 'infertility' would apply to her either. Kathleen and Tom were both raised in conservative religious households. She and Tom both came from large families; their parents now have 27 grandchildren. It wouldn't appear that there are any problems with reproduction. How could there be?

Kathleen and Tom made careful plans before their marriage so that they would be prepared for a family: researched career choices, accepted positions with growing software companies in the Seattle area, purchased a house in an area where the schools were highly recommended. Why couldn't she get pregnant? Two years passed, then three before they were able to bring themselves to discuss their apparent infertility and learn about the mind-boggling possibilities in fertility treatments, none of which they wanted to discuss with their seemingly problem-free siblings.

After a long journey through tests and research, Kathleen and Tom had two children through in vitro fertilization. The process was lengthy and expensive. After months of painful injections to boost her egg production, Kathleen underwent procedures to have 6-8 eggs removed. The eggs were then fertilized with her husband's sperm in a Petri dish, and the resulting embryos were incubated for several days in a carefully controlled environment.

Four blastocysts (embryos with about 150 cells) were implanted back into Kathleen. They were each smaller than a period at the end of a sentence, had no heartbeat and could not develop into a person without successfully implanting in a womb. Statistically, one out of every four implanted embryos results in a full-term pregnancy, but the first time none of Kathleen's embryos developed into a fetus. They had to repeat the procedure two more times. There were six potentially good embryos remaining when Kathleen became officially pregnant. The extra embryos were frozen and stored in a special tank.

At holiday gatherings no one would ever know that Kathleen and Tom's children had been conceived any differently than any other cousin running around the back yard. Yet the path to parenthood had put them at odds with their faith, which does not approve of in vitro fertilization because of the risk to potential embryos and because of the use of technology for procreation. However Kathleen and Tom felt sure that they were meant to have children. Although there is more initial uncertainty with IVF than with a regular pregnancy (*What if the embryo doesn't implant? What if all four of them do?*), once the pregnancy is advanced it is no different than any other. Occasionally Kathleen and Tom remembered the extra embryos and were glad: if they decided to have a third child it would be possible. Then Kathleen learned that she was pregnant, after the years of fertility treatments she didn't even know to recognize the signs. Her doctor told her that it is not uncommon for women with infertility problems to be somewhat "cured" by having children. Their family is now complete. Their older children are five and three years old now, and the baby has just been born.

But they still have these extra embryos and the insurance company has notified them that the $500/year storage fee is no longer covered. The notification letter came in the same mail with an invitation to yet another school fundraiser.

However, the insurance company also included a letter from a research institute citing a desperate need for embryos. That's when Kathleen learned that the debate over stem cell research involves her family, and also the family of her best friend.

The letter stated that there are potential medical breakthroughs that can be made on virtually every disease known if researchers are able to use stem cells in their research. According to the information (from Harvard's Stem Cell Center, no less) there are only about twenty-two stem cell lines available to researchers who use federal funding for their research. At the same time, an estimated 400,000 unused embryos are in storage tanks throughout the United States. Most stem cell lines have been grown on feeder cells derived from mice. The paper cites the need for more human embryonic stem cell lines. In the letter, one researcher wrote about his personal stake in creating more stem cell lines for research. His son and daughter have Type 1 diabetes and his son is insulin-dependent. He believes that scientists will be able to cure diabetes, perhaps using stem cells to grow insulin. Kathleen's best friend Clare has three children, and her oldest was diagnosed with diabetes when she was just two years old. Clare practically devotes her life to raising money for diabetes research, in addition to trying to make her daughter's life seem as normal as possible. Kathleen knows that if Clare had embryos to donate she would do it in a heartbeat.

Kathleen and Tom find time to sit down together to discuss their options. The embryos belong to them, but they do not plan to use them. The storage cost is $500 per year, which would pay for a lot of new shoes. They hate the idea of their embryos, the embryos similar to the ones that became Caitlin and Tom Jr., being discarded as medical waste. They believe those embryos have the possibility of life, even if they do not have heartbeats. The position of their religion is that these stem cells are sacred and should not be used for research. The Stem Cell Center states that due to the current government policy, they are not able to use any Federal dollars and must rely on private funding. The Center also notes that they will make the stem cell lines available to any scientist in the field. They estimate that from 350 donated embryos they could double the number of stem cell lines available for research.

Kathleen makes a list of possible actions to take, and then they read over the page again that gives specifics about research. It says that the embryos have been frozen for varying amounts of time; they do not always survive thawing. Those that survive may not develop into a blastocyst. The letter states that cells generated by the embryos cannot be identified with the donors. Kathleen and Tom talk about their own children and how they would feel if they were diagnosed with a disease. In the past they have talked about whether they would donate their organs if anything happened to them. They believe that life is sacred and that it begins at conception. Tom suggests that they pay the $500 for another year, while they learn more, but Kathleen feels strongly that it is time for them to decide how they feel about stem cell research. Her children are like miracles, exhausting, but miracles. What research led to in vitro fertilization breakthroughs that allowed them to be born? She thinks to herself, "the embryos don't have heartbeats and they could help to save lives. But don't we have a duty to protect them? What should we do?"

To Think About

What are the options for Kathleen and Tom?

What do you think Kathleen and Tom should do with the extra fertilized eggs? Why?

Which bioethical principle is given the most weight in your solution?

Explain why you chose that ethical principle.

Please see NWABR's Stem Cell Curriculum, available online at www.nwabr.org, for a full classroom lesson based on this case.

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Case written by Peggy Sturdivant

Bioethics Curriculum Online

Access Excellence
http://www.accessexcellence.org
Entering 'bioethics' into the search brings up many useful pages related to teaching bioethics.

Bioethics.net
http://www.bioethics.net/
http://highschoolbioethics.org/
Site of the American Journal of Bioethics/University of Pennsylvania. Updated news stories, bioethics background, and an active bioethics blog. This site also provides a high school bioethics resource.

EIBE Units
http://www.eibe.info/
Collections of classroom activities from the European Institute for Biotechnology Education, including a variety of experimental protocols, practical activities, role-plays, information and debates. The units are very clearly written, provide information at an appropriate level, and are well-illustrated. Both biotechnology and bioethics units are featured.

Ethics Updates - University of San Diego
http://ethics.sandiego.edu
Ethics Updates is designed primarily to be used by ethics instructors and their students. It is intended to provide updates on current literature, both popular and professional, that relates to ethics. It provides classic texts, case studies, background on theory and helpful resources such as ethics lecture videos.

Genetic Science Learning Center
http://gslc.genetics.utah.edu/
Many helpful resources on stem cells, genetic disorders, and ethical issues.

Howard Hughes Medical Center
http://www.hhmi.org/research/bioethics/
A web page and companion free DVD on bioethics. Features research ethics, animal research scientific integrity, and genetic alteration. The HHMI web site also has additional resources related to topics such as stem cells.

The High School Human Genome Project at the University of Washington
http://hshgp.genome.washington.edu/teacher_resources/modules.htm. Provides a case study and a bioethical decision-making template. The Ethics curriculum module, which can be downloaded, allows students to explore ethical issues related to the genetic testing of Huntington's disease.

Human Genome Project Information - Ethical, Legal and Social Issues
http://www.ornl.gov/hgmis/elsi/elsi.html
The U.S. Department of Energy (DOE) and the National Institutes of Health (NIH) have devoted 3% to 5% of their annual Human Genome Project (HGP) budgets toward studying the ethical, legal, and social issues (ELSI) surrounding availability of genetic information. This represents the world's largest bioethics program, which has become a model for ELSI programs around the world.

Kennedy Institute
http://www.georgetown.edu/research/kie/
http://highschoolbioethics.georgetown.edu/
The Kennedy Institute is a teaching and research center offering ethical perspectives on major policy issues. It is the largest university based group of faculty members in the world devoted to research and teaching in biomedical ethics and other areas of applied ethics. The Institute also houses the most extensive library of ethics in the world, the National Reference Center for Bioethics Literature; produces bibliographic citations relating to bioethics for the online databases at the National Library of Medicine; and conducts regular seminars and courses in bioethics. The high school bioethics project has developed case studies on topics of interest to secondary school teachers and students.

National Center for Case Study Teaching in Science
http://ublib.buffalo.edu/libraries/projects/cases/case.html
The University of Buffalo has many examples of case study teaching in science - try a search with 'ethics'

NIH Bioethics Resources on the web
http://www.nih.gov/sigs/bioethics/
A great place to start for background information and various positions on a variety of bioethical issues.

Online Ethics Center for Science and Engineering
http://onlineethics.org/index.html
This site contains a wide variety of useful resources and links on research ethics, moral leaders in science and engineering, women and minorities in science and engineering, and codes of ethics. Especially useful are the links for precollege curriculum, ethics in the biological sciences (which features a unit on the ethics of animals and research) and the case studies involving research ethics.

President's Council on Bioethics
http://www.bioethics.gov

Your Genes, Your Choices: Exploring the Issues Raised by Genetic Research.
http://ehrweb.aaas.org/ehr/books/index.html
This resource is published online by the American Association for the Advancement of Science and features 8 case scenarios easily adapted to a classroom setting.

Wellcome Trust
http://www.wellcome.ac.uk/
The mission of the Trust is 'to foster and promote research with the aim of improving human and animal health'. Reflecting the profound impact today's research will have on society, the Wellcome Trust also seeks to raise awareness of the medical, ethical and social implications of research and promote dialogue between scientists, the public and policy makers. *LabNotes* provides teachers with up-to-date information on research findings in biomedicine and the social and ethical implications of this research. The Wellcome Trust commissioned the Institute of Education, London, to find out the importance teachers attached to the study of socio scientific issues and how they went about tackling such issues. A summary of the research —*'Valuable Lessons: Engaging with the social context of science in schools'* - was published in July 2001.

Additional Bioethics Resources Online

Socratic Seminar Websites:

http://www.paideia.org
The National Paideia Center has several excellent resources for teaching using seminars. We especially recommend their "Active Thinking Through Dialogue" publication, available to order online.

http://www.studyguide.org/socratic_seminar.htm
Description of Socratic Seminar, pre-seminar activities, discussion of difference between debate and dialogues, student guidelines, and seminar rubric.

http://www.middleweb.com/Socratic.html
Lynda Tredway.
Educational Leadership. Discussion about how to engage middle level students in intellectual discourse through Socratic Seminars. Connects students to ethics by having them examine ethical quandaries and to develop moral principles.

http://www.ncsu.edu/literacyjunction/html/tutorialsocratic.html
A tutorial on Socratic Seminars with explanation organized around pre-seminar activities, during-seminar activities, and post-seminar activities, stressing the "essential question" approach.

Films

Bioethics Films Available for Loan from the Kennedy Institute of Ethics, bioethics@georgetown.edu
http://bioethics.georgetown.edu

Commerical Films Dealing with Bioethics Topics
http://bioethics.georgetown.edu/hsbioethics/
Select bibliographies, then commercial films dealing with bioethics topics

Further Reading

Beauchamp, T., and J. Childress, The Principles of Biomedical Ethics, Oxford University Press, 2001. 454 p.

This book has long been used as an introduction to bioethics. It is based on the approach developed by Beauchamp and Childress entitled "principlism" and focuses on the principles of autonomy, beneficence, nonmaleficence, and justice. The book refers to cases (in an appendix) and provides a very good comparative overview of the varieties of philosophical theory and evaluates each theoretical approach from the authors' perspective. The authors provide great references and address "moral character" (virtue theory); ethical theory is very much a part of this introduction. Used frequently at a college level.

Pence, Gregory, Accounts of Cases that Have Shaped Medical Ethics, with Philosophical, Legal and Historical Backgrounds, 3rd ed. Boston: McGraw-Hill, 2000. 509 p.

Dr. Pence examines some of the seminal cases in bioethics, those that advanced the development of the field and are still talked about and taught today. The legal and legislative process in bioethics and philosophical debate and perspectives may be covered on a variety of topics - removal of respirators, artificially provided nutrition and hydration, anencephalic infants, etc. Used both at high school and undergraduate level.

Veatch, Robert M., The Basics of Bioethics, 2nd ed. Upper Saddle River, New Jersey: Pearson Education, Inc., 2003. 205 p.

Dr. Veatch is a scholar at the Kennedy Institute of Ethics and is one of the early educators and ethicists in the field. He offers an introduction that addresses major issues in bioethics, but with a good dose of the ethical theory that grounds the discussion. The book contains descriptive text, history, case studies, definitions, some contemporary treatment of the issue, and a bibliography for each chapter. The second edition has been updated to track developments in clinical medicine and ethical theory. This book has been used successfully in both elective high school courses on bioethics and at the undergraduate level.

Anthologies

Beauchamp, Tom and Walters, LeRoy, eds. Contemporary Issues in Bioethics, 6th ed. Belmont, CA: Wadsworth, 2003. 800 p. [ISBN 0-534-58441-1]

Mappes, Thomas A. and DeGrazia, David, eds. Biomedical Ethics, 5th ed. Boston: McGraw-Hill, 2001. 707 p. [ISBN 0-07-230365-4]

Munson, Ronald, ed. Intervention and Reflection: Basic Issues in Medical Ethics, 6th ed. Belmont, CA: Wadsworth/Thompson Learning, 2000. 891 p. [ISBN 0-534-52039-1]

Shannon, Thomas A. An Introduction to Bioethics. Mahwah, NJ: Paulist Press, c1987, 1997. 189p.

Steinbock, Bonnie; Arras, John D.; and London, Alex John. Ethical Issues in Modern Medicine, 6th ed. Boston: McGraw-Hill, 2003. 830 p. [ISBN 0-7674-2016-0]

Teays, Wanda and Purdy, Laura M., eds. Bioethics, Justice, and Health Care. Belmont, CA: Wadsworth/Thomson Learning, 2001. 683 p. [ISBN 0-534-50828-6]

Other Useful resources

Crigger, Bette-Jane, ed. Cases in Bioethics: Selections from the Hastings Center Report. Third Edition. New York: St. Martin's Press, 1998. 295 p.

Levine, Carol, ed. Taking Sides: Clashing Views on Controversial Bioethical Issues. Ninth Edition. Guilford, CT: McGraw-Hill/Duskin, 2001. 380 p.

Reich, Warren Thomas, ed. Encyclopedia of Bioethics. Revised Edition. New York: Simon Schuster Macmillan, 1995.

Journals

Hastings Center Report (bimonthly journal) published by the Hastings Center, Route 9D, Garrison, NY 10524; tel. 845-424-4040; fax. 845-424-4545. Short, scholarly articles; case studies and commentaries

Journal of Bioethics
Online at http://www.bioethics.net/

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Northwest Association for Biomedical Research

100 W Harrison, North Tower, Suite 430
Seattle, Washington 98119