

Ethics & Medicine

An International Journal of Bioethics



Vol 27:2
SUMMER 2011
ISSN 0266-688X

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 info@bioethicspress.com
 www.ethicsandmedicine.com

SUBSCRIPTIONS

Ethics & Medicine is published three times a year by The Bioethics Press, Ltd. Subscriptions may be obtained and address changes can be made with the publisher at the address above.

The mission of *Ethics & Medicine* is to reassert the Hippocratic consensus in medicine as seen through the lens of the Judeo-Christian tradition on the conviction that only a robust medical professionalism is able to withstand the challenges of emerging biotechnologies and their clinical applications.

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association with:

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EDITORIAL

HOW WOULD YOU LIKE TO DIE?

C. BEN MITCHELL, PHD

The institution where I teach had the fortunate opportunity to welcome Gilbert Meilaender to our campus recently. Meilaender is the Duesenberg Chair of Christian Ethics at Valparaiso University, and he served on the President's Council on Bioethics from 2002-2009. He was also a doctoral student under the inimitable Paul Ramsey, whose legacy in medical ethics readers of this journal will surely know. Meilaender is at once both sage and winsome, brilliant and humble. His talks corresponded with a forthcoming book project: *Facing the Dying of the Light: Perspectives on Aging and Dying*.

Meilaender opened his series of lectures by reflecting on the perennial question "How would you like to die?" Most people today, he suggested, would answer with one word: "Suddenly!" Generally speaking, we want to live as long as we can, at the peak of our powers, and then fall off a cliff, as he put it. Doubtless, he is right about contemporary attitudes toward death. If we have to go, let it be quickly and painlessly.

I heard Professor Meilaender against a backdrop of *Transcendent Man*, the new documentary of the life of inventor-scientist Ray Kurzweil. The documentary makes one thing crystal clear: Ray Kurzweil hates death. Though I am not a psychologist, it seems obvious from comments Kurzweil makes that he was traumatized as a young person when his father, a professional musician, died suddenly. Kurzweil laments that he was not able to prevent his father's death because our technology is not sufficiently developed—yet. So, Kurzweil has kept all of his father's belonging in storage, including pictures, ledger books, musical scores, etc., in hopes of one day recapturing his father's consciousness through artificial intelligence technologies. Kurzweil even believes that some AI machine one day will be able to scour from his own brain memories of his father to add to the rich pastiche of his father's life as it is recreated. Kurzweil thinks that he will live long enough to make a "copy" of himself so he can move one step closer to the so-called "Singularity" and a technologically-achieved immortality.

Thus, if these two views are representative, people would prefer to die either suddenly or not at all. What struck me while Meilaender was speaking—and he said as much during his lectures—is that it was not always so. Historically, most people have seen death as unavoidable and sudden death as particularly lamentable. Although no one relished extended suffering, the terminal condition gave opportunity to make peace with others, with God, and perhaps with death itself. Death was not welcomed in most cases, but its inevitability meant that "dying well" meant not merely dying as painlessly as possible but dying with one's accounts in order, as it were.

Perhaps these two scenarios—either sudden death or no death at all—both miss this important aspect of human experience. On the one hand, sudden death robs us of the opportunity to reconcile ourselves where necessary so that we come to the end of our days with some resolution in our lives. On the other hand, if current experience is any teacher, indefinitely extended lifespan would mean we would be tempted to persist unreconciled to

those with whom we are at odds. In both cases, we might miss one of the most important aspects of being human. It's at least worth thinking about, it seems to me. **E&M**

GUEST COMMENTARY

REMEMBERING DIGNITY

CHRISTOPHER BECHTEL

On December 1, 2010, the Scottish Parliament emphatically rejected the possibility of euthanasia and assisted suicide, voting 85 to 16 against the “End of Life Assistance (Scotland) Bill”. One of the reasons for this outcome was the inability of those in favour of the bill to use the human dignity argument to their advantage. This was because, both inside and outside Parliament, their understanding of the concept of human dignity was persistently challenged.^{1,2,3}

The apparent intractability of the debate about human dignity is not new, but the recent discussions in Scotland offer a fresh opportunity to explore the role of human dignity in medical ethics—a role which can be divided into two broad categories. Some view human dignity as essentially synonymous with autonomy. Others, however, understand human dignity to be vital to all meaningful discourse about human ethics.

The Dignity Debate

In a now-classic article, Ruth Macklin claims that the concept of human dignity offers nothing of value to medical ethics.⁴ Citing several examples, she contends that dignity is confusing shorthand for the more useful concepts of autonomy and respect. Macklin’s terse article concludes that eliminating the concept of dignity would serve medical ethics by allowing clearer concepts to prevail. If Macklin’s examples and argumentation were to hold, her conclusion would be valid. To put it differently, if dignity is merely a cipher for more precise terms, its demise is no great loss.

In broad agreement with Macklin are several parties that have vocally contributed to the debate about end of life assistance. American journalist Derek Humphry penned the bestselling book *Dying with Dignity* in order to explain the ethics and legality of euthanasia. In the UK, the Voluntary Euthanasia Society changed its name to Dignity in Dying, and in the state of Washington, USA, the “Death with Dignity Act” legalised physician-assisted suicide in 2008.⁵ While disputing Macklin’s contention that dignity is worthless, these supporters of assisted dying concur that human dignity is generally equivalent to the notion autonomy and that it is something that can be lost depending on a person’s quality of life or rational capacity. According to these supporters, a person only maintains his or her dignity by exercising a choice.

Maintaining Dignity

Responding to these accounts, several thinkers have argued that dignity belongs in meaningful ethical dialogue.⁶ However, the future of the concept depends on adoption of a refined usage that distinguishes between types of human dignity.⁷ These can be separated into two broad categories. The first, “inherent dignity”, is an unalterable, necessary quality that belongs equally to all members of humanity. This sense of dignity agrees with the UN Universal Declaration of Human Rights which affirms in its

preamble “the inherent dignity and...the equal and inalienable rights of all members of the human family” as “the foundation of freedom, justice and peace in the world”.

In contrast, the second type of dignity is “non-inherent”, meaning it is a contingent, variable condition upon which a person merits various honours. Non-inherent dignity may be gained or lost depending on behaviour or social standing, but inherent dignity is permanent and inseparable from personhood.

Under both definitions, dignity is an intangible quality. Dignity requires people to act in a certain way toward others. Whether inherent or non-inherent, dignity motivates actions, such as respectful behaviour. But, to be clear, dignity itself is not something to be conferred. Thus, for example, the inherent dignity of a homeless man motivates a hospital to treat him for frostbite in the winter, and the non-inherent dignity of an eminent professor compels a research student to ask questions with humility.

However, the key difference between the two concepts is this: inherent dignity is irreducible, transcending the honour or respect that varies according to social position or behaviour, while non-inherent dignity is bound to specific circumstances. These simple distinctions allow human dignity to act as a universalising concept without also denying the notion that some non-inherent dignity may be lost.

An illustration may clarify these distinctions. Suppose a malicious army general ruthlessly destroys a town of anarchist peasants. When eventually captured, the general is arraigned on charges of crimes against humanity and banished to prison. At the trial, jurors hear the prosecution argue that the general violated the dignity of the peasants. At the same time, the general himself complains that the prison’s hard bed and mundane food are beneath his own dignity.

The jurors recognise that, regardless of provocation, the general should not have massacred the peasants. He was obligated to behave decently toward them and to find more humane ways of exercising his authority. The jurors also see why the general, accustomed to a feather bed and sumptuous cuisine, would expect prison officials to behave deferentially toward him by catering to his preferences. In both cases, the concept of dignity underlies expectations for certain actions.

The inherent dignity of the peasants requires the general to act with justice rather than rash violence. Although the peasants violated a civil code, they must be treated with respect on account of their inherent dignity. As the jurors discern, the inherent dignity of the peasants is not synonymous with “respect”. Instead, it is the foundation and justification for respect. The general disregarded this inherent dignity by barbarically massacring the peasants, and thus he deserves heavy-handed condemnation.

Ironically, it is the general’s own inherent dignity which requires that any eventual punishment he receives should meet certain standards of civility. For example, physical or psychological torture would constitute disregard for his inherent dignity by subjecting him to unnecessary and unreasonable pain. More humanely, however, the judge may opt to strip the general of his rank. If demoted to private or corporal, the general would lose the dignity of a high-ranking officer. His fellow soldiers would then no longer be obligated to act towards him with the respect required of a general (e.g., no mandatory salutes). Armed with a binary concept of human dignity, the jury can legitimately convict the general. However, without distinguishing between inherent from non-

inherent dignity, both the general's guilt and his subsequent demotion are difficult to substantiate.

With Macklin, someone might argue that the concept of inherent dignity is unnecessary, since a crime against humanity is simply a disregard for autonomy or a failure to act with justice. However, while such a crime may indeed evidence disdain for an individual's rights, the question remains why autonomy should be respected in the first place, and the concept of inherent dignity answers the question. Respect for autonomy is a behaviour that flows out of awareness of inherent dignity.⁸ The concept of dignity—and particularly the two-pronged view advocated here—promotes and secures ethical treatment for the whole of humanity through inherent dignity and, at the same time, makes sense of the common understanding of a variable notion of non-inherent dignity.

Contemporary medical ethics needs the concept of human dignity but not the simplistic, confused concept criticised by Macklin. As already suggested, by recognising the concept of inherent dignity, medical professionals afford themselves a rational foundation for ethical treatment of all patients. Without this concept, on the other hand, there is no justifiable principle for equality in treatment.⁹

Moreover, practitioners of medical ethics must remain vigilant to maintain the distinction between these concepts of dignity lest inherent dignity be subsumed as part of non-inherent dignity. The great danger, of course, is that inherent dignity could be viewed as a non-permanent quality, dependant on mental or social status. For example, supporters of assisted suicide programmes commonly commit this category mistake in assuming that the loss of autonomy is tantamount to a loss of dignity.

Conclusion

Recent deliberations in Scotland have once again raised the question of whether the concept of human dignity is relevant to the debates about euthanasia and assisted suicide. Not surprisingly, some experts have concluded negatively, arguing that the concept is confusing, if not irrelevant. Others, though, see human dignity as the foundation of meaningful dialogue about the end of life.¹⁰ Though further research is needed, a promising and useful way forward is to distinguish between inherent and non-inherent dignity.

Endnotes

- 1 End of Life Assistance (Scotland) Bill Committee Report, The Scottish Parliament, November 2010, <http://www.scottish.parliament.uk/s3/committees/endLifeAsstBill/reports-10/ela10-01-vol1.htm>.
- 2 Official Report, The Scottish Parliament, Col. 31042, 1 December 2010, <http://www.scottish.parliament.uk/business/officialReports/meetingsParliament/or-10/sor1201-02.htm#Col31042>.
- 3 J. Balfour, 'Dignity of life trumps the choice of the ill to end their suffering', *The Scotsman*, Friday 5 March 2010.
- 4 R. Macklin, 'Dignity is a useless concept', *British Medical Journal* 327 (2003): 1419-1420. Macklin, of course, is by no means alone in this position. For other accounts see e.g. P. Singer, 'All animals are equal' in *Unsanctifying Human Life* (ed. H. Kuhse; Oxford: Blackwell, 2002), 90.
- 5 The Oregon law passed in 1997 bore the same title.

- 6 E.g., D. Schroeder, 'Dignity: Two riddles and four concepts', *Cambridge Quarterly of Health Ethics* 17 (2008): 230-238.
- 7 E.g., R. Andorno, 'Human dignity and human rights as a common ground for a global bioethics', *Journal of Medicine and Philosophy* 34 (2009): 223-240. Andorno distinguishes dignity as inherent and moral. However, both the term 'moral' as well as Andorno's application of the term are of limited value. Broadening Andorno's second category to 'non-inherent' enables the term to encompass the full range of activities that recognise a dignity other than a universal, inherent dignity. See also D. P. Sulmasy, 'Human dignity and human worth' in *Perspectives on Human Dignity: A Conversation* (ed. J. Malpas and N. Lickiss; Springer, 2007), 9-18.
- 8 Importantly, regard for inherent dignity does not guarantee respect for autonomy. In France, for example, the influential Conseil d'Etat ruled that local governments may outlaw activity that violates human dignity, e.g., dwarf tossing, even if an individual voluntarily consents to the activity. On this particular case see the UN Human Rights website: http://tiny.cc/unher_dwarf tossing.
- 9 Cf. S. Killmister, 'Dignity: not such a useless concept', *Journal of Medical Ethics* 36 (2010): 160-164.
- 10 E.g., D. P. Sulmasy, 'Human dignity and human worth' in *Perspectives on Human Dignity: A Conversation* (ed. J. Malpas and N. Lickiss; Springer, 2007), 9-18.

CLINICAL ETHICS DILEMMAS

ADOLESCENT CONFIDENTIALITY: AN UNEASY TRUCE

MARY B. ADAM, MD, PHD, FAAP

Editor's Note: *This column presents a problematic case that poses a medical-ethical dilemma for patients, families, and healthcare professionals. As it is based on a real case, some details have been omitted in the effort to maintain patient confidentiality. In this case, the doctor discusses her experience from the retrospect of the unanswered question.*

Column Editor:

Ferdinand D. (Nick) Yates, MD, MA; Professor of Clinical Pediatrics, State University of New York at Buffalo

Question

How should a physician respond to multiple-party claims of authority?

Case Presentation

Some Fridays are more memorable than others. This one started with a pile of phone messages, and my nurse said that the one on top was urgent. The patient – age seventeen – said she had to come in immediately and talk: “I’m desperate. And please do not let my mom know. I might be pregnant, I need your help.” The patient’s mother had also called. I requested that the nurse make arrangements without notifying the mother, as I would call later.

The patient arrived during my lunch hour, since it was the only time available, and was frantic, as she was certain that she was pregnant. Her menstrual period was late, and, indeed, urine testing confirmed her pregnancy. Based on the timing of her last period she was about eleven or twelve weeks along. The patient said that her mom would pressure her to get an abortion. We talked for a long time about what she wanted, if the father of the child was to be involved, and the challenges to be faced. I also informed the patient that her mother was already aware of something as she had also called to talk to me. I asked how she would like me to handle things with her mother since I would need to return her phone call from earlier in the day. The patient already knew that her mother was suspicious and recognized that the discussion was both necessary and appropriate. The patient was willing to see a counselor and an obstetrician on the following Monday for confirmation of dates via ultrasound. She wanted me to help her speak with her mother and said that I could invite her to come in Monday for a joint discussion. The patient thought letting things settle over the weekend was the best course of action. The immediate next step was for me to tell her mother that we would all talk the following week and that her daughter was medically fine and getting all the care she needed.

Things seemed to have the potential to move forward, and just as I was about to take a quiet moment at the end of the day to call the teenager's mother, the assistant medical director for our multi-specialty clinic stormed into my office. He irately informed me that there had been a severe patient complaint that he needed to address with me immediately. Apparently, a patient of mine was being denied access to care in violation of her reproductive rights, and what did I think I was doing? A mother who had called about her daughter was livid because she was certain her daughter was almost at the twelve-week limit when an abortion could be done locally and with less risk to her daughter. She said that she had informed the director "that the treating physician was making things worse." Somewhat shaken, I asked the name of the patient, and, sure enough, it was the adolescent female with whom I had spoken this morning. I informed my medical director that I had seen the patient, that she was pregnant, and that she had told me she wanted to keep the baby. When he heard about the proposed plan of action, he felt less concerned about the issue of "denial of access to care" and – given the full picture – did not have risk management concerns at this time.

Discussion

This case documents four distinct perspectives regarding patient care: that of the patient, the physician, the patient's parent(s), and the medical administration. In some cases, these perspectives exhibit little divergence, but on most occasions our greatest medical conundrums arise from the conflict of two or three of these positions.

This case highlights the physicians often face in practice when they seek to balance the competing and sometimes conflicting notions of confidentiality, veracity, and fidelity. The pregnant teenager (even as a minor) has certain mandated privileges – state and federal – that entitle her to a variety of medical care services without the consent or even the knowledge of her parents. How does the treating physician resolve conflicts between the parent's values and those (rights or values) of their minor child? What does it mean to respect the family's values? What harm may come to the child as a result of disrupting a stable system of social support provided by the family? What does an individual do if he or she, as the physician, has a conflict with the course of action chosen by a patient or a parent or, on the other hand, if the employer has a conflict with the medical course of action the physician deems appropriate? The physician's fiduciary responsibility consists of transparent competent care that is free of coercion.

In this case, the professional duty to the patient for confidentiality was in potential conflict with the duty to tell the parent the truth. In general, this special challenge is more common in pediatrics, in which case the pediatrician has a legal obligation to the parents (or legal guardian) and a moral obligation to appropriately protect the patient's privacy. In pediatrics, parents are assumed to be appropriate decision makers for their children and most agree that parents deserve wide latitude in determining what is best for their children. This includes determining their own families' values and teaching the children according to these principles. Respecting a family's values means recognizing that parents have the primary role in helping to define what constitutes their child's well being and their child's understanding of the "good." Our legal system provides options for physicians in cases in which parents are incompetent. In addition, we also understand that young children are unable to make decisions. However, the fact is that children outgrow their dependent states. As maturation progresses and a child's ability to

understand information increases, the parent has a moral obligation to honor the child's specific perspective, which may lead to a conflict between the parents' notion of what is best for the child and the child's own view of what is best for himself. This potential conflict occurs in multiple domains, not just in the area of reproductive health.

There was little doubt, in this case, that the mother (as the patient's parent and guardian) had "guessed" what was going on, given her calls to the physician and the medical director. However, this does not diminish the challenge of supporting the patient who is not a mature minor, is not of legal age, and disagrees with her mother on the best course of action. This patient stated, "My mom will kill me if I do not have an abortion," (an ironic comment as two would be killed instead of only one). But in fact, the mother was presumably primarily concerned about the emotional and social chaos, the profound disappointment, and the sense of loss the news would bring, rather than the actual physical harm. The effort to schedule time with both mother and daughter provided an opportunity to both support the patient and to fully disclose difficult information. In settings in which a physician has concerns about addressing these conflicts, inviting a behavioral therapist and social worker to attend the meeting can be very helpful.

This case also illustrates the conflicts that might arise (at the administrative level) between employers and physicians who have moral objections to a legally available procedure – such as abortions. The physician does have the duty to engage with patients and families about controversial matters such as abortion. This does not mean that the physician must bow to requests to carry out an action that she finds morally offensive. In this case, my moral objection to abortion was known to both my employer and my patients. Not surprisingly, full disclosure minimizes but does not eliminate the potential for conflict. As this case demonstrates, the mother was concerned enough about my position on abortion to call the medical director, and the daughter felt welcome enough to request my assistance. In my opinion, the moral integrity of a physician is reinforced by being open about her moral boundaries and not hiding information. If there is an irresolvable conflict, physicians retain the right to transfer a patient to the care of another competent physician. Respect of patients and their families is a cornerstone of the therapeutic relationship, and respect should be maintained even in settings in which physicians may disagree with a patient's or family's decision.

This case also highlights the need for strong communication skills, something which is, sadly, more often "caught than taught" in medical school curriculums. Effective communication addresses the cognitive need of both the parent(s) and patient to know and understand as well as the emotional needs of both parties to feel known and to be heard and understood. While effective communication cannot resolve all conflicts, it can substantially impact the physician's ability to actively demonstrate care for a patient even if there are areas in which a physician entertains the possibility of transfer of patient care.

Denouement

To the chagrin of this physician, the patient was lost to my follow-up care. I do not know if the infant's life was allowed the opportunity to flourish or if it was terminated.

Editor's Comment

This case represents how a particular medical-ethical problem can generate perceived individual autonomy and directed persuasion from each of several perspectives. Each viewpoint – parental (often protective, but occasionally overbearing), physician (often supporting patient rights, but sometimes engaging in personal right of conscience discussions), and administration (citing legal and societal claims) – will each align with some aspect of the patient's best interest and simultaneously may aggrandize its specific perspective.

The challenge for the practicing physician is to direct a clinical path that exercises professional fiduciary care for the patient while offering proper respect for parental authority and appropriate adherence to the administrative underpinnings, along with being able to exercise her individual right of conscience. This process generally demonstrates compassion and may conjure up compromise, but it always demands genuine care for the patient. The physician's responsibility is to the patient who asks for his or her help and somehow the physician needs to honor that relationship even in the face of substantial challenges from other people and aspects of the patient's healthcare needs.

Suggested Reading:

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GREY MATTERS

THE ORIGAMI BRAIN: FROM NEURAL FOLDS TO NEUROETHICS

WILLIAM P. CHESHIRE, JR., MD

Starting from an uncut paper square and proceeding through a series of careful folds, origami master Brian Chan has fashioned a detailed replica of the human brain, which he displays on his website.¹ Art imitates nature as tissue paper patterns the shape of living tissue. The fine wrinkles and fragile creases of Chan's extraordinary model depict the brain's intricate ordering and delicate construction.

Nature also imitates art. The development of the nervous system begins with a tiny layer of cells, and as they grow, they undergo an elaborate sequence of foldings that culminate in the structure of the brain. The resemblance to origami is evident as early as the beginning of the third week of human life. Like a crease in a piece of paper, a narrow groove known as the primitive streak appears on the surface of the embryonic ectoderm. Expanding toward the primitive streak, the lateral edges of the slipper-shaped neural plate gradually elevate to form the neural folds. By the fourth week the neural folds approach each other at the midline and fuse, rendering the neural tube. The narrow portion of the neural tube organizes into distinct layers of cells that form the spinal cord. The cephalic portion of the neural tube broadens, and its cusp – the cranial neuropore – undergoes closure, sealing off the dilatations that form the brain vesicles. A series of flexures in the brain vesicles demark the prosencephalon, mesencephalon, and rhombencephalon. With further growth, the prosencephalon bends sharply, dividing the telencephalon from the diencephalon. By the fifth week the telencephalon divides into two outpocketings that will form the cerebral hemispheres, whereas the diencephalon will form the thalamus, hypothalamus, optic tracts, and posterior portion of the pituitary gland. A deep furrow divides the diencephalon from the mesencephalon, which will form the midbrain, and a fissure separates the mesencephalon from the rhombencephalon, which will form the pons, cerebellum, and medulla.²

By seven months, the cerebral hemispheres are organized into the frontal, parietal, occipital, and temporal lobes, which are named according to the bones of the skull that overlie them. Several deep grooves outline the lobes of the brain. The medial longitudinal fissure divides the left and right cerebral hemispheres from one another. The lateral sulcus divides the frontal and parietal lobes from the temporal lobe, and the central sulcus divides the primary somatosensory cortex from the primary motor cortex.

In addition to prominent frontal lobes, a distinctive anatomical feature of the human brain in comparison to that of other animals is its highly convoluted cerebral cortex. The cerebral cortex consists of a sheet of neural tissue folded in such a way that its large surface area fits within the confined space of the cranium. Ripples of gyri and sulci shape a surface of undulating cortical folds. By adulthood, the cerebral hemispheres enfold 2500 cm², which is 1.4 times the surface area of the front page of the *Wall Street Journal*.^{3,4}

Myriads of paper folds would be needed to model the microscopic interior of the brain. Replicating the manifold twists and turns of 100 billion neurons sharing 160 trillion synapses would challenge the most nimble-fingered origamist. This level of structural intricacy, though impressive, is less remarkable than the brain's functional capacity. From a folded sheet of neurons emerge such high-level cognitive faculties as perception, language, abstract reasoning, and creative expression. From this grey matter also comes the skill to guide hands to fold paper into precise geometric shapes that transform ideas into visual metaphors and delight the imagination.

Origami, the Japanese art of paper-folding, is about creating graceful paper sculptures in three dimensions. To fold a sheet of paper is to specify its shape by making a linear crease across its surface. Ethics is about drawing lines that distinguish the boundaries of acceptable and unacceptable conduct in the moral dimension. In Japanese culture, origami also symbolizes peace.⁵ Likewise, ethics is concerned with living in harmony with others. As Chesterton observed, "Art, like morality, consists in drawing the line somewhere."⁶ Insofar as origami and ethics both concern relationships that can be represented geometrically, the spatial language of origami may provide some insights for neuroethics.

Whence does neuroethics derive its moral folds? Are they prearranged by natural conditions that are part of an objective moral order, or are folds intentional and subject to the choice of the individual or group? Is the topography of morality more distinct than a crinkled sheet, the defining features of which are left to the imagination? For ethical contours to be meaningful, they must have consistency, coherence, and be subject to investigation and understanding. Creases must be consequential, and folds must express real character.

An origami theory of neuroethics would recognize in moral topography both given and chosen folds. Fixed ethical boundaries would be like the gridlike creases in a paper roadmap, which must be refolded along prespecified lines. As yet undecided ethical boundaries might be as open as a flat piece of blank tissue paper. In life, most ethical decisions will lie somewhere in between.

The possibilities for folding may be infinite, but they are not unbounded. Some folds are logically prohibited. For example, it is impossible with a single fold to divide a sheet of paper into three equal parts. Other folds are futile. Once a fold is made, the options for further folds are constrained to those that respect the geometry of existing folds. The organizing principles and existing folds in the realm of moral reality are critical to recognize. Just as efforts to fold contrary to the shape of things will degrade their form, decisions heedless of the contour of moral topography are ultimately harmful or ineffective.

Neuroscience provides a bottom-up approach toward discerning the topography of neuroethics. Progress in neuroscience consists of an unfolding of increasingly precise and detailed descriptions of the nervous system and its interactions. The reductionistic methodology of neuroscience, which examines the nature of complex systems by studying its parts, has proven extremely useful in elucidating how the brain works.

Within the last century, science brought biology within the fold of chemistry just as chemistry had been brought within the fold of physics. Neuroscience now enters the fold of the exact sciences, and, with it, psychology, philosophy, and spirituality, all of

which are subject to increasingly detailed descriptions in terms of brain function.⁷ The neurobehavioral processes corresponding to perception, awareness, belief, emotion, empathy, the formation of moral sentiments, ethical reasoning, motivation, and decision-making all draw upon specific cortical circuits that can be localized through functional brain imaging techniques.^{8,9} These cortical circuits, which relate to uniquely human experiences and behaviors, consist of highly interconnected clusters of neurons exchanging information that is chemically encoded at the molecular level.

Technological convergence refers to the paradigm in which the distinctions that separate scientific disciplines break down, allowing for advances in one field to inform new ideas in others. The National Science Foundation report *Converging Technologies* outlined a vision for the unification of cognitive science with the other sciences. Its opening sentence reads: “We stand at the threshold of a new renaissance in science and technology, based on a comprehensive understanding of the structure and behavior of matter from the nanoscale up to the most complex system yet discovered, the human brain.”¹⁰ One of the proposed NSF research programs would be a “Human Cognition Project to understand the nature of the human mind”¹⁰ by means of natural mechanisms. In a similar vein, Francis Crick writes of “the scientific belief” that “our minds—the behavior of our brains—can be explained by the interactions of nerve cells (and other cells) and the molecules associated with them.”¹¹

If Crick and others are correct that the human mind is fully reducible to the molecular behavior of the brain, then neuroethics also reduces to neurochemistry and morality to molecules. Michael Gazzaniga, for example, argues for a brain-based neuroethics, writing that he would like to support “the idea that there could be a universal set of biological responses to moral dilemmas, a sort of ethics, built into our brains.”¹² A complete theory of neuroethics could, in principle, be attained by mapping out the moral folds of the brain through technology that counts and measures the blips that denote the behavior of grey matter.

The neurobiological case for moral realism may be reasonably criticized for violating the naturalistic fallacy in that it attempts to derive an “ought” from an “is” by defining values in terms of facts. William Casebeer, in pressing the case for a brain-based neuroethics, identifies the goal of showing “that norms are natural and that they can arise from and are justified by purely natural processes.” “If this can be done,” he adds, “then the naturalistic fallacy is not actually a fallacy (it merely amounts to saying that you don’t have a good naturalized ethical theory yet).”¹³ This is not, of course, a scientific claim based on evidence but a wishful assertion based on the assumption that more facts will finally close the gap between categories that are indubitably irreconcilable.

Much can be affirmed about a brain-based theory of neuroethics. Because neuroscientific findings can be empirically tested, measured, and stated objectively, its conclusions in regard to ethics can be universally acknowledged. A brain-based neuroethics also recognizes all of humanity as belonging to a common moral community.

The aspiration to identify a brain-based neuroethics, however, fails to furnish a complete account of human nature. Though accurate, it cannot be the whole truth about the mind and its place in the moral universe. There are truths that are not empirically verifiable, qualities that are nonquantifiable, and realities that are irreducibly

subjective. Such a theory lacks any external standard by which to judge a given behavioral phenomenon as good or evil. It would also seem to permit the option of using biotechnology to reengineer the brain into a posthuman entity by reshaping its moral folds in some artificial image.¹⁴

As in any art form, paper folding has practical limits. Some simplification would be needed for an origami model of even a single cerebellar Purkinje neuron with its 200,000 finely arborizing dendritic fibers.¹⁵ Folding may also have philosophical limits. For example, does the architecture of the brain mathematically delimit boundaries to human knowledge? Within those boundaries, are there things that cannot not be known?^{16,17} Are there aspects to human dignity that, because they cannot be measured, cannot be manipulated? Outside those boundaries, what grand indecipherable thoughts might lie beyond human comprehension?¹⁸

Folded paper always points beyond itself. Each fold is a finite line along a path whose direction extends infinitely. Where folds converge, they make a corner that also points beyond itself. An exquisitely folded work of origami implies the existence of one who conceived the figure and did the folding. Neuroethics relates richly to art and is firmly grounded in neuroscience. Neuroethics also points beyond itself to purpose and meaning in human life beyond description.

Recognizing in morality a transcendent source, Feinberg and Feinberg argue that “certain acts are inherently right and others inherently wrong. They are so because they either reflect or do not reflect the character of the God who made the world and all in it.”¹⁹ Whereas the origamist divides paper and the neuroscientist divides neurons, the Scriptures declare that God’s creative power is such that he divides light from darkness,²⁰ waters from waters,²¹ and soul from spirit.²²

A brain-based neuroethics ultimately is a paper ethics, a morally thin construction that tears under stress and collapses under pressure. A genuinely human neuroethics, by contrast, rises beyond its stature and reflects a wisdom not entirely its own.

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IS FREE WILL AN ILLUSION?

JOHN R. MEYER, MS, LTD, STD

Abstract

Neuroethics is a burgeoning field of scientific–philosophical investigation that is becoming a genuine interdisciplinary area of study. This is because neuroscience offers a unique window into what it means to be human, explaining, at least to some extent, the important difference between the brain and the mind. Among the many fascinating topics in neuroethics is the neuroscience of free will and the nature of moral responsibility. Many contemporary philosophers are considered compatibilists, arguing that human beings are not truly free because their actions are completely determined by the material processes of the brain. However, if conscious willing is illusory or simply an epiphenomenon, both compatibilist and incompatibilist accounts of free will are erroneous. A great deal of scientific evidence and philosophical reflection suggest that, despite all the difficulties we experience in explaining free will, we do not unconsciously cause our actions.

Key words: neuroethics, free will, quantum mechanics, mental causation

Introduction

One of the more fascinating areas of study in neuroethics concerns the neurobiology of free will. Several neuroscientists claim that the experience of free will is just an epiphenomenal illusion, with underlying neural processes causally sufficient to explain the mental states that correspond with volitional action. Others contend that consciousness is simply the state neurons are in when a person is alert, with any temporal gap during the decision-making process reflecting the accompanying molecular activity located at lower levels of the brain. Personal experience suggests, however, that our states of mind are not completely determined by neural events. Indeed, material determinism fails to acknowledge the numinous qualities of the mind and thus threatens to change what it means to be human.

Here I speculate on the significance of the temporal gap separating pre-action neural activity from the conscious awareness of decisions to act, reviewing and critiquing Benjamin Libet's seminal studies in this area. Then I comment on the feasibility of recourse to quantum mechanics to explain the indeterminacy of free will, arguing that mental causation cannot be explained in exclusively physical terms. While external evidence provides ample proof of regularities or patterns in natural events, as well as predictability among the succession of events in nature, the causality associated with free will is unique. Since the top–down causation of free volitional activity cannot be fully explained in terms of material functionalism alone, we must invoke philosophical reflection on the nature of what it is to be human to explain free will.

Competing Philosophical Accounts of Free Will

Those who deny the existence of free will view human thoughts, desires, decisions, and intentions as causally impotent phenomena, even though our common appeal to moral

responsibility in societal life rules out material determinism *tout court*. In point of fact, if a person were not causally responsible for her actions, just about everything she believed about her as personal and free would be false.¹ In addition, the very idea that the future is completely predetermined by the laws of nature and assorted antecedent neural conditions is incompatible with the everyday experience of free will, an activity that enables us to choose between alternative possibilities and exercise control over our actions. So Thomas Nagel alleges that the only way to consider free agency properly is to see human action “as a basic mental or more accurately psychophysical category—reducible neither to physical nor to other mental terms.”²

Authors who defend a compatibilist account of free will situate the psychological sensation of freedom in the matrix of material determinism. A typical compatibilist formula states that x chooses freely to ϕ if and only if the relevant antecedents of the choice leave the ϕ -ing up to x . To be more precise, an agent acts freely when she identifies with her motivational states in a reflective way and then endorses her desires and selected actions in the absence of external coercion. An interactive version of compatibilism maintains that the impersonal influences of the laws of nature, along with the agent’s subjective beliefs and desires, allow for genuinely free choices and actions. Thus there is no need to frame free will in terms of substance (or property) dualism, sometimes referred to as libertarian or incompatibilist free will. The human being is not the union of two substances (like a rider and horse), or even the union of a man and an animal (such as the centaur).³ Rather, she is a unified composite substance, somewhat analogous to wax and the shape given to it by a stamp.⁴ Incompatibilist theories can be non-causal, event-causal, and agent-causal in kind. In the first case, intentional action begins *ex novo* with a basic mental action or desire. The event-causal account allows for a modicum of agent control, good reasons for acting, and the possibility of not performing a proposed action. And the agent-causal view denies that free acts can be reduced to events, since agents can give reasons to explain why they acted in a certain way, even though reasons are not the actual cause of free actions.⁵

The literature in the area of cognitive neuroscience is truly immense, and I do not pretend to be able to summarize it in such a brief essay. My approach to the topic will therefore be quite selective and limited. First, I review the groundbreaking experiments of Benjamin Libet on the so-called Readiness Potential, which supposedly demonstrates that subconscious mental states control volitional action. In this connection, I point out some interpretative problems with Libet’s data and propose alternative ways of understanding his findings. Second, I discuss some problems with a reductionist concept of functional brain activity in which mental states are deemed to be nothing more than mechanistic, lower-level, molecular operations that cause what appear to be free acts. Third, I rehearse what proponents of quantum physical theory propose may be going on at the subatomic level in living organisms—a randomness and probability that allows for the presence of free will in human beings. Then I outline various views of top-down mental causation, suggesting that some but not all of them are useful for explaining free will. Finally, I describe the relation between free will and natural causality, offering a novel way of depicting personal agency in the context of lower-level molecular activity.

Free Will and the Readiness Potential

Libet found that when subjects were asked to flick their wrist as soon as they noticed a fast-moving dot of light arcing across the face of a clock, a negative electrophysiological potential appeared at the vertex of the scalp *before* conscious awareness of the decision to act. Libet called this the “readiness potential” (RP), borrowing the expression from Hans Kornhuber and Lüder Deecke.⁶ The RP appears 550–700 milliseconds (ms) prior to electromyographic activity (EMG), whereas conscious awareness of the urge to move takes place around 200–300 ms before the EMG. Since an experimental subject only realizes her decision to act *after* the RP spike, Libet concluded that a person is merely informed about a subconscious decision to act and is not directly involved in making that decision. Of equal interest, the will can intervene prior to executing a motor act, allowing for a conscious veto of the proposed action. For Libet, this meant that conscious free will is limited to controlling whether a voluntary act occurs, with its initiation following a “bubbling up” of unconscious initiatives in the brain and the conscious will simply selecting which conceivable action(s) to perform.⁷

Several alternative interpretations of this data have been offered since then, including the possibility of potential report biases. For instance, when participants are asked to identify the location of a moving dot on a computer screen, respondents tend to project its path farther along the dot’s trajectory and overestimate its final position.⁸ What is more, awareness time varies as a function of clock speed, with responses shifted forward in time at higher clock speeds. If these experiments were repeated at different clock speeds, the time differences between the onset of the RP, subject awareness of the intention to move, and the onset of movement would probably differ from Libet’s original results.⁹ Further, the exogenous stimulus control Libet employed in these experiments is suspect because exogenous and endogenous stimuli are qualitatively distinct.¹⁰

One could argue that the electrophysical cerebral activity preceding conscious awareness is precisely what we would expect to see before volitional actions, with the variation in mental processing correlated with the complexity of the task at hand. In Libet’s experiments, subject reports about the intention to act concerned well-rehearsed rote responses, representing the general states of arousal or the preliminary motor information needed to prepare for a predetermined movement. In fact, conscious awareness depends on antecedent cerebral preparation, and this subliminal neural activity is often unconscious.¹¹ Since more complex volitional actions require additional time to process, the simple voluntary movement used in Libet’s experiments is not suitable for evaluating an intentional movement driven by complex conscious decisions.¹² The experimental subjects may have actually wondered whether they were experiencing an urge to act, a thought about when to act, or an anticipation of acting in the near future.¹³ Given the fact that subjects were instructed in advance *not* to flex their fingers, they did not actually veto an *intended* motor action but performed a prearranged abortive act.¹⁴

On balance, then, Libet’s studies may have had little to do with intention awareness as such. On the contrary, test persons were simply instructed to introspectively monitor an internal trigger, which could have been nothing more than the *sensation* of an ambiguous threshold of muscle tension induced by an anticipated action. The half-second lag-time between the onset of the RP and awareness of an intention to act reflects the interval of precursory neuromuscular activity preceding pre-determined modes of

acting, and a purposive causal agent represents possible courses of action to herself only when there is more at stake.¹⁵ On this point Robert Sokolowski writes:

In making a choice, I must distinguish sharply between the purpose I seek and the action I now perform; I must articulate a whole into discrete and heterogeneous parts; I must recognize the parts as parts, and I must concomitantly hold all those parts together in an articulated and synoptic whole—the whole that is governed by the purpose and populated by its intermediary steps.¹⁶

Rational self-determination entails the capacity to reflect on reasons for acting, being willing to revise one's entertained desires in light of critical normative reflection. It seems possible that Libet confused the conscious decision to act with the state of the brain *by means of which* one becomes aware of a decision to act. Also, because his subjects were *conscious* of what to do, they may have (unconsciously) delegated the initiation of requested tasks to sub-personal mechanisms capable of rapid responses.¹⁷

Materialism and Functional Brain Activity

Just as we do not blame a clock for telling the wrong time but look to the clockmaker or the clock-reader for the fault, unconscious neural activity alone does not appear to be responsible for aberrant moral behavior. Part of the problem with Libet's interpretation is his working premise: that materialism is self-evidently true. Functional dependence is not the same thing as ontological identity, and the fact that brain activity is necessary for mental acts does not necessarily mean these two activities are equivalent.¹⁸ This distinction becomes clearer when we consider the qualitative aspects of phenomenal consciousness, or qualia, which defy reduction to matter and do not always correlate well with functional states and subjective experiences.

We all have a grasp of the subjective or phenomenal character of such states as the visual experience of orange, the feeling of anger, the sensation of being about to sneeze. Our grasp of what it is like to undergo these and other experiential states is supplied to us by introspection. We also have a grasp, albeit an incomplete one, of what goes on objectively in the brain and the body. But there is, it seems, a vast chasm between the two.¹⁹

Emotions play an important role in ethical thinking as well, and certain molecular changes correlate with diseased psychological states. Consider the emotional apparatus of the psychopath, who is irresponsible in behavior and indifferent toward others. Scientific evidence indicates that the amygdala, a brain structure that propagates the aversive emotions of fear and anxiety, is compromised in people with this personality disorder. Functional magnetic imaging (fMRI) demonstrates a correlation between reduced amygdala response and high scores on Hare's revised Psychopathy Checklist, and neuropsychological studies show that the orbito-frontal cortex may also be involved.²⁰

While high-resolution brain scans provide a refined mapping of the neural substrate of the mind, this cerebral "blueprint" is not reducible to the mind's functional features, for the human intellect possesses qualitatively novel properties that are not exhibited by the physical properties of the brain. Nonetheless, Michael Gazzaniga still claims that neuroimaging data enables us "to read" human intentions: "there could be a universal set of biological responses to moral dilemmas, a sort of ethics, built into

our brains.”²¹ In reality, the voxels that constitute a brain scan represent the shape of what *is*, not what *ought* to be done. Furthermore, real-time fMRI brain scans are not a visual representation of thought but digital displays of material activity that precedes and accompanies conceptual thought. So even though fMRI studies have been used to analyze preferences, altruism, social cooperation, and the intention to deceive or lie, their practical value concerning free ethical behavior is uncertain at best.²²

Quantum Physics and Free Will

John Searle believes that quantum physical theory enables us to elaborate an event-causal account of free will because it employs probabilities to describe the random behavior of sub-atomic particles. On this reading, higher organizational structures emerge from random, lower-order, molecular activity in predictable ways.²³ Jaegwon Kim, by contrast, argues that the novel properties arising from basic material particles completely transcend their constituent properties, and the laws governing simpler systems have no predictive value with respect to emergent properties. Indeed, many physical phenomena are independent of predictable fundamental laws, with complex organizational structures and activities acquiring an identity that rises above the parts from which they are composed.²⁴

Here it is interesting to point out that the Hodgkin-Huxley equations that describe neural impulses cannot simply be reduced to the laws of physics. These equations depend upon the organization of proteins that mediate the potassium and sodium current across axon membranes as well as the geometric structure of the nerve fibers, giving rise to new laws that govern the dynamic activity of nerve impulses at a higher level of functionality than physics or chemistry. What warrant, then, do we have to assume that human behavior is derivable from neurobiological laws rather than some higher-level organizing/action-selecting principle?²⁵ Although top-down agent causation must be related to the indeterminist micro-level laws of nature, an agent’s causal power has to be different *in kind* from the events that go to shape that power. Consider the fact that a headache causes me to desire pain-relief. While the sensation of pain and the wish for its alleviation are determined by distinct brain states, emergence of the desire for pain relief requires an additional causal influence: *I must decide* to take an aspirin to obtain pain relief.²⁶ For all intents and purposes, an agent-causal account of free will rules out the possibility that we merely experience the voluntary actions we perform.

Yet another problem with recourse to quantum mechanics to explicate free agency is the fact that material randomness is insignificant in larger physical systems like the brain. So, even if sub-atomic indeterminacy did affect matter on the macroscopic level, an apparently intractable dilemma still remains. “If I am not free, despite the fact that I can do what I want when I want, how does the fact that sometimes – due to a random event – I *fail* to do what I want when I want to enhance my freedom?”²⁷ In short, the indeterminacy of sub-atomic phenomena would *reduce* my freedom, and free choices would not be under the agent’s control. As J. J. C. Smart quips: “I would feel that my freedom was impaired if I thought that a quantum mechanical trigger in my brain might cause me to leap into the garden and eat a slug.”²⁸

A further difficulty arises when authors fail to distinguish between biological predispositions and free choice, what scholastic authors used to call the *voluntas ut*

natura and *voluntas ut ratio*. Patricia Churchland, for instance, does not differentiate between involuntary neural seizures and voluntary abusive behavior in discussing the correlation between material and volitional activities:

Imaging techniques (functional MRI) showing unusually low levels of activity in the orbital cortex can help us predict that a person is depressed. If a person has a mutation in the gene that normally produces the enzyme mono-amino oxidase A (MAOA), and if he has also had an abusive upbringing, we can reliably predict that he will display irrationally violent and self-destructive behavior. An electroencephalogram (EEG) in which electrodes are placed on the scalp, can detect brain changes that predict the imminent onset of an epileptic seizure.²⁹

On this score, Walter Glannon reminds us that we hold people responsible for their behavior, not their brains or minds. “We hold persons responsible on the basis of the mental states that issue in their actions, and these states are generated and sustained by the brain. But the content of those mental states, the external events to which they are directed, cannot be explained entirely by reference to their neural correlates.”³⁰

Actually, deterministic neuroscientific explanations are relevant when we have reason to believe behavior is unintentional or irrational, and this is especially true when a person entertains an *ersatz* conviction. A person with the paranoid belief that an alien from Mars is pursuing him may act in bizarre ways, such as hiding behind a bush when approached by a stranger. Evidently, this is not a rational action, for the content of the belief is clearly false.³¹ Even if there is a definite correlation between neurophysical and psychological states, that association cannot tell us how a neurophysical state relates to a good act or a positive psychological state.³² Interestingly in this regard, Martin Heisenberg claims that *intrinsic* behavioral modules functioning independently from sensory input are a sign of free will, and the activation of these modules is based on an intricate interplay between chance and the cerebral laws of nature. Then again, the very examples Heisenberg provides, such as the grasp reflex of a baby, undermine this interpretation, for reflexes are involuntary reactions to something external to the agent.³³

These considerations indicate that if the choices we make were strictly indeterminate, free acts would just be random, arbitrary, capricious, and totally inexplicable. One possible way to describe downward causation in terms of quantum states is to envisage a broader high-level system influencing the otherwise indeterminate events at the quantum level. George Ellis, for example, contends that the constituent particles at the micro-level, albeit devoid of individual properties as such, are influenced by extrinsic factors that modify their native indeterminacy and give rise to “entangled states” that would allow for the emergence of free will. In consequence, besides possible cooperative effects among the constituent parts themselves, top–down causality could confer a certain order on the underlying elementary particles.³⁴

Top–Down Mental Causation

When someone deliberates over what to do in a particular situation, she usually elaborates reasons to explain her final decision. If there is no time to consciously deliberate, the person may not be fully aware of the reasons she chose a particular action. Moreover, many habitual ways of acting are explained *after* the fact, either in order to

assuage one's conscience or to justify the chosen behavior to others. This does not mean that agent causality can simply be reduced to the order of material causality, however.

Suppose an apple falls on the table before me, and I ask the question "Why?" The right way to answer is by citing a cause: it fell because the breeze dislodged it. By giving causal explanations, we are automatically ordering events in space and time, and the causal relation itself is intrinsically temporal. But suppose that you throw an apple onto the table before me, and I ask the question "Why?" The question now has quite another sense. In the normal case – that is, the case where it is not asked *of* you, but addressed *to* you – the question looks for a justifying reason, not a cause. Why should you throw this apple down before me? The answer might be that I deserve it, or that it would be good to eat.³⁵

If an agent employs efficient causality to bring about an action that transcends material causation and requires a reason to be fully explained, we cannot conclude that conscious mental states are merely higher-level system features of the brain. The agent must cause her free actions, even if reasons as such are not causative. And while beliefs and desires explain why an agent acts, she must exercise a distinctive executive power in order to act, and the operations of this power are not fixed by prior physical events.

When a human being acts in a fully rational way, she chooses an action in light of beliefs and desires, even though she is not caused to act by those beliefs and desires. This is most evident when a person weighs the pros and cons of different courses of action, evaluating the various *reasons* for acting one way or another. The vying reasons do not sort themselves out on their own, of course, nor does any one set of reasons cause the final chosen action to take place. Also, the fact that a choice is not determined by prior events or by certain mental states does not mean it is an arbitrary occurrence, for one chooses among assorted sources of evidence to deliberate with— reasons for or against the contemplated action— and then determines how to direct her thoughts. Once a specific course of action is decided upon, she moves her body to obtain the desired end. Does this mean free will is a quasi-divine attribute? Roderick Chisholm has led some readers to think so: "each of us, when we act, is a prime mover unmoved."³⁶ Owen Flanagan's allegation that Chisholm advocates God-like creative abilities *ex nihilo* is a rhetorical ruse, yet he is surely correct to ask how free will could be embedded in the context of material causation. "We think of free actions as unforced, as not involving compulsion to do what we don't want to do, but that is very different from thinking that free actions occur with no constraints or totally outside the causal nexus."³⁷

An agent-causal theory of action holds that the acting subject normally has an intention in mind with pertinent content and that the exercise of active control over personal actions is a causal phenomenon. Jonah Lehrer neglects this key aspect of decision-making in discussing how a naval officer decided to shoot down an unidentified flying object that threatened a Coalition battleship during the Persian Gulf War. The radar operator recognized something unusual about a blip on the radar screen, and this anomaly led him to infer that he was seeing an incoming Iraqi missile. Lehrer explains this by saying that dopaminergic neural cell firing altered in response to an unusual radar pattern.³⁸ But, as Richard Taylor explains, something more is at work in such situations.

If I believe that something not identical to myself was the cause of my behavior—some event wholly external to myself, for instance, or even one internal to myself, such as a nerve impulse, volition, etc.—then I cannot regard the behavior as being an act of mine, unless I further believed that I was the cause of that external or internal event.³⁹

Agents possess an active power in virtue of a particular set of natural properties that contribute to their causal powers in a way that differs from and transcends simple event-causation. Even if macro-properties do emerge from the microstructure of the brain, reasons for acting are not causal in the usual sense of the term. As Timothy O'Connor puts it, "I produce my decision *in view of* those reasons, and could have, in an unconditional sense, decided differently."⁴⁰ In other words, we have the power to cause an effect or to *refrain* from causing it, and this power reflects the fact that reasons are not causes when they are not heeded.

Nancey Murphy alleges that a person's ability to subjugate behavior to the dictates of reason reflects the higher human capacity to evaluate prospective actions and to act for abstract ideas like justice, and this mental mechanism can be explained by adopting a non-reductive, physicalist view of agent autonomy.

My recommendation is to say that when a person acts on the basis of considered goals and principles, without undue biological or social interference, she has become the author of her own acts and ought to be described as acting freely. This again, is free will understood as autonomy, but without the unrealistic expectation of total autonomy.⁴¹

Murphy speculates that the dynamic neurobiological system acts as a downward cause by *constraining* or *selecting* lower-level parts of the body's constituent functional parts. This explanation of human free will is somewhat suspect, however, for its principal aim is to preserve traditional concepts of moral responsibility and associated social practices.⁴²

David Chalmers alleges that, even if the physical world is causally closed, conscious awareness and deliberative operations could supervene on the physical in a *natural* way, with supplementary properties being described with psychophysical laws.⁴³ Interesting in this regard, there is empirical evidence of downward mental–physical causation in certain psychiatric states. PET scans reveal that special cognitive therapy in individuals with Obsessive Compulsive Disorder alters the physical structure of neural circuitry, indicating that our minds do influence the physical structures of the brain.⁴⁴ In light of these empirical findings, John Haldane's portrayal of the human being as a psychophysical substance is intriguing. Just as the formal structure of an object is communicated to the senses and then to the intellect in knowledge acquisition, a person's intentions may *inform* or *structure* her desired action by means of the efficient causality of matter. On this interpretation, there are hierarchies of organizational complexity in the brain, with various levels of structuring principles subsumed under a single psycho-physical form. This depiction of the mind–body relation agrees with the observation that all biological entities have an organizing principle of some kind, with each of the non-substantial parts structured in a definite way by that principle.⁴⁵ And if the mind shapes the body and its functions in both intentional and volitional terms, it is not an added attribute but *the*

defining principle of a human being.⁴⁶ So the brain may not be simply the integrator of various body systems but the *modulator* of a pre-existing somatic unity.⁴⁷

Some formal structural ordering is required in material causation as well, for efficient causality alone neither implies determination nor excludes randomness, and the presence of such reliable patterns are of critical importance in scientific research. Indeed, it is the patterns of regularity in nature that make scientific inquiry possible, for only then can a scientist legitimately assume (and predict) that this regularity will remain in the future.⁴⁸ The convergences we observe in biological organisms are quite remarkable, something akin to ripples of water converging on a central point in a pond rather than diverging from the central point of propagation. Furthermore, in view of the fact that time-reversed backward causation is impossible in rational human beings, the mind must impose patterns of activity on the brain based on deliberative volitions.⁴⁹

Natural Causality and Free Will

Daniel Wegner alleges that the conscious thoughts which come to mind prior to acting are mere *previews* of possible actions, and these mental representations rise to the level of consciousness as the end-result of unconscious processes. Free will is therefore just “a conscious experience that may only map rather weakly, or perhaps not at all, onto the actual causal relationship between the person’s cognition and action.”⁵⁰ Despite the fact that we experience ourselves as making conscious decisions, intending specific ends, and acting in particular ways, the impression that a particular thought causes a specific action is based on inferences, and such judgments are always open to question. In support of this opinion, Wegner cites the movements of the planchette on an ouija board, table turning, automatic writing, and pendulum divining. But, as Roger Scruton reminds us, we must ask the right kind of question in cases of this kind.

When the judge asks me why I put arsenic in my wife’s tea, he will not be satisfied by the response, “[b]ecause electrical impulses from my brain caused my hand to reach for the bottle and tip it into the waiting teacup”, although that may be a true answer to the question “why?” construed as scientists construe it, as a request for the cause. For it is an answer *of the wrong kind*. My original answer to the judge was absurd not because it was false but because it removed my action from the sphere of judgment and described it in terms that make no reference to it as *mine*.⁵¹

Simple rote tasks often involve unreflective decision-making processes, such as which hand I use to answer the telephone, or the exact phrase I use to ask for a cup of coffee. All the same, if you put your mind to it, it is possible to control some unconscious actions, such as learning to voluntarily control heart rate and blood pressure. One can also learn to direct thoughts in positive ways in order to avert obsessive patterns of cognition, manage panic attacks, and ward off bouts of depression.⁵² And the capacity for off-line action simulations or rehearsed behavioral scenarios indicates that the person *as a whole* is an agent of thought and action, not some fictive inner self located inside the brain.⁵³

Harry Frankfurt distinguishes self-reflective free will from freedom of action, with second-order desires enabling a person to reflect critically upon spontaneous impulses and wishes by forming second-order volitions that can modify her valuation of goods and redirect self-chosen goals. Lynne Rudder Baker bases her compatibilist explanation

of moral responsibility on Frankfurt's hierarchical concept of the will. If an agent is able to conceive her desires as truly her own, she cannot be the mere conduit of deterministic forces beyond her control. After all, this person produces intentions that shape the causes of what is done by modifying her first-order desires.⁵⁴ Clearly, this kind of mental reflection is not always operative, as many routine actions align themselves with one's general view of life, being second nature and pre-determined to some extent. And so the very process of deliberation is indicative of immaterial mental activity, since it concerns general descriptions of possible events. Moreover, we learn general concepts and terms from others, and these transcend purely material or physical configurations in space and time, not being an instance of efficient causation *per se*.⁵⁵

All things considered, explaining the compatibility of free will with the regnant scientific theory of material determinism appears insoluble, primarily because compatibilist accounts of the mind–brain relation reduce intellectual and volitional activities to epiphenomena. Allen Wood explains the problem in this way: “The basic objection to compatibilism is that if we are nothing but a product of our physiology plus external causal influences, then we cannot possibly be the sort of beings who could be the cause of our own actions entirely from ourselves – that is, freely.”⁵⁶ Flanagan's neo-compatibilist version of free will is not completely convincing either, for he fails to reconcile free will with natural causality, even openly admitting that his proposal is a purely naturalistic account of volition. While common sense notions of free will demand more than compatibilist interpretations of freedom can provide, at least these notions respect the complexity of the psychological and rational processes we experience. Actually, the advocates of an inter-actionist concept of freedom gain some empirical support from Libet's experimental findings, if not his interpretations of the same, because the conscious mental event of a decision to act in a specific way coordinates several mutually independent neural events that induce a specific pattern of activity.⁵⁷

Conclusion

In bringing these various considerations to a close, it is important to recognize that a search for the neural correlates of consciousness assumes that the brain is the sole source of all mental activity— an assumption that has led several cognitive neurobiologists to abandon a global vision of self-consciousness. A critical step forward in this field would entail elaborating a unitary or holistic explanation of brain function and mental activity. Free action does not necessarily demand the suspension of natural laws or quasi-deterministic material processes, even though it does require the personal intervention of an agent. Whenever a human being acts, he or she intervenes in a causal sequence of events that could have yielded a different result from that which came to pass.

When I decide to blink my eyelid rapidly, I am intervening into the biological or physiological “laws” that normally cause my eyelid to blink according to a particular organic regularity. My intervention into the organic regularity has the effect of making the eyelid blink faster or slower than it normally would without the intervention. In so intervening, I am not violating the laws of nature, but I am utilizing and deploying them in accordance with my overarching intention. But at no point is my action capable of successful completion in the total absence of the structures of organic, physical reality. Action supervenes on nature but cannot occur in its absence.⁵⁸

The action of an intentional, self-guided, purposive agent cannot be reduced to material phenomena alone. A higher-level organizing principle must be at work, conferring unity, structural order, and purposive agency to the entire organism. And this necessarily entails something more than ‘editing’ the products of direct physical causation.⁵⁹ The all-encompassing agent is inclusive and imparts order, ‘reaching down’ as it were, through its myriad chemical and physical structures, in order to deploy that infrastructure to carry out the intended purpose.

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WOULD TREATMENT ALLOCATION ACCORDING TO AGE-CONTINGENT DEPRECIATION BE ETHICAL? A DIALYSIS & TRANSPLANTATION PARADIGM

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Abstract

In an era dominated by calls for healthcare reform, reasonable and just medical costs merit everyone's attention. A perplexing expense is renal replacement therapy (RRT, CKD5 or End Stage Renal Disease/ESRD). It includes patients with permanent kidney failure—either on dialysis or transplanted. It has garnered disproportionate review because of its substantial Medicare reimbursement. RRTs have experienced a 57% increase in costs from 1999-2004, approximately 7% of Medicare's total annual budget. In fact, there are reasons why ESRD might become the cost-cutting paradigm for reformers, and age may be the focal point. RRT's demographic is older; in fact, the fastest growing segment is persons 75 years of age or greater. Budgetary considerations could foster future discussion of rationing. Limiting geriatric renal failure patients' access to ESRD therapies based solely on age is unjust. Would an empiric focus on medical benefit be more prudent? Applying medical benefit criteria would be an ethically acceptable approach. Recent studies have demonstrated that dialysis initiates a decline in functional status in this age group. ESRD, accompanied by concurrent comorbidities (ischemic heart disease, dementia, peripheral vascular disease), predicts survivals on dialysis no better than conservative strategies without. Bodily depreciation consequent to aging does not tolerate dialytic interventions well; therefore, there may not be medical benefit in elderly with CKD5. However, in contrast, age per se in the RRT population is not a predictor of poorer outcomes after transplantation. Furthermore, survival in this age group is better with earlier transplantation as opposed to either no intervention or dialysis. Studies suggest that age matching donors and recipients (old to old) may also improve overall access to organs, thereby increasing quality of life and longevity for older CKD5 persons. Rationing and its attendant cost-cutting can represent either ethically informed stewardship or the unfair imposition of social value criteria. This era may provide an opportunity to carefully consider medical benefit as a mitigator to healthcare costs and emphasize palliation rather than death hastening—only if advancing years per se are not selected as a rationale to limit care.

As the debate surrounding healthcare reform continues, controversial boundaries have already been drawn. Atul Gawande observed in a prominent national periodical, “cost is the specter haunting healthcare reform.”¹ He reminded everyone that medical costs have doubled over the last decade, absorbing 18% of every dollar spent. One thing is certain: costs will continue to increase in an era inhabited by high technology, market-driven medicine, dubbed by some as medicine’s “Corporate Transformation.” Recent iterations of health care reform will probably not succeed in slowing that rise. Therein lies the rub. The nefarious word rationing is *the* contingent of rising costs, often packaged within a veneer of social value

criteria. It continues to be asked, “Which groups should bear the brunt of cost cutting?” When the answer crystallizes, the common refrain has been “let’s limit monies expended on the elderly.”² The particular genre leading to this proposal gained prominence with Daniel Callahan’s “Setting Limits.” Although medical benefit is an acceptable criterion, it is frequently abandoned in lieu of age per se. Cognizant of the ethical quagmire consequent to any model proposed for rationing, one might inquire whether there are other solutions to soaring costs. Could it be that excessive costs are hidden within therapies that obtain meager or no medical benefit across particular age groups? Furthermore, might there be correlations between certain medical benefits (or lack thereof) and the natural, physical depreciation associated with aging? This approach utilizing medical benefit criteria is categorically and ethically different than limiting access to therapies solely based on age.

At the risk of oversimplifying healthcare reform, expensive therapy specifically directed at end stage renal disease (renal replacement therapy, RRT, and transplantation) will be evaluated ethically in the context of medical benefits, natural physical depreciation with age, and the elderly. As a specific, albeit limited example, it may be prudent to determine whether dialysis is *prima facie* beneficial to the geriatric population. That is one ethical question. Since dialysis is not the only therapeutic modality applied to RRT, age and its impact on transplantation must be evaluated as well. So, it will also be asked whether the allocation system for transplantable kidneys respects age and is sensitive to medical benefits as well. Juxtaposition of these two ESRD therapies in the context of age and medical benefit is the primary subject of this paper. Although RRTs represent merely a portion of contemporary medical expenses, they might serve as a paradigm to be extrapolated to other burdensome and/or inefficacious treatments across a spectrum of ages. Ethical extension of this paradigm to other treatments will be discussed later.

Scope of the Problem: Costs of the CKD Epidemic That May Lead to Cost Cutting

Chronic dialysis, and less so transplantation, consume a disproportionate share of resources when compared to other diseases and treatments.³ RRT has become necessary for approximately 339-400 per one million individuals, and the size of that specific cohort has been increasing. Diabetes mellitus dominates etiologies responsible for CKD and is also reaching epidemic proportions. Approximately 4% of individuals with both diabetes and CKD consume 13.4% of expenditures allotted to the entire RRT group.⁴ With CKD in general, the financial burden to Medicare and non-Medicare providers for renal replacement therapies has been estimated at \$20.1 and \$12.4 billion dollars annually respectively.⁵ Despite rich investment of monies, the USA, which has one of the highest rates of ESRD globally—coupled with the highest expenditures per ESRD patient—manifests some of the worst outcomes.⁵ U.S. dialysis patients live approximately one-third to one-sixth as long as age- and gender-matched individuals.⁶ Compared to persons afflicted with cancer or AIDS, CKD5 persons fare worse.⁶ In fact, the five-year CKD5 survival is 38%, roughly half of that in people with cancer.⁶ However, in regard to costs, there was a 57% increase in the Medicare ESRD budget for ESRD between 1999 and 2004, comprising of 6.7% total expenditures. Some might ask, “Should we pay for that type of outcome?” Another way in which to frame escalating costs would be factor in the recent Medicare Part D Benefit package.⁷ The average number of medications taken by ESRD patients is 10 to 12 per day. The number includes expensive parenteral staples

of ESRD therapy such as erythropoietin. Expansion of Medicare benefits seems to eventuate in disproportionately rising expenses for ESRD. These expenses reside in the realm of dialysis.

From the perspective of age and kidney transplantation, patients above the age of 50 years comprise 60%, and above 65 years, 17% of individuals wait listed for kidney transplants.⁸ Costs, as well as comparisons to dialysis outcomes for transplants will be provided later.

It is important to place this discussion into a general budgetary framework. In the next year, for the first time, government funded programs will account for more than half of total medical spending in the U.S.⁹ This financial prospectus also predicts that by 2020, one in every five dollars spent in the US will go towards healthcare. Medicare's financial stressors will only get worse, and Medicare pays for ESRD across all age groups, not just in those older than 65 years. These facts have spawned an ethical inquiry: Why waste money on the old when you can spend it on the young?

An Ethical Reframe: Dialysis Efficacy in the Elderly by Medical Benefit Criteria

As mentioned earlier, RRT rationing discussions seem to inevitably focus on the elderly. A review of the demographics of renal replacement therapy may address why that is the case. The fastest-growing ESRD segment is comprised of individuals 75 years-of-age or older.⁵ Study of this group can also demonstrate that costs of ESRD increase with age. Furthermore, costs increase further if age plus diabetes mellitus with heart failure—not atypical comorbidities in this group—are present.⁵ As a result, a corollary has been drawn: Society can save the most money by withholding care from those groups increasing disparately in both volume and cost, and for ESRD, clearly that group is older. In essence, “Since their life expectancy is short, why spend the money?”

In reframing the discussion of age and renal replacement therapy, it should be asked rather, “What are the medical benefits of ESRD therapies (dialysis and/or transplant) in geriatric populations when compared to younger cohorts and when compared to conservative therapy (that is, care without dialysis)?” Those questions have been approached from a number of reliable perspectives.

Between 1998 and 2000, approximately 3700 nursing home residents in the United States in whom functional status (i.e. ability to perform activities such as walking, bathing, dressing, getting out of bed, and using the toilet) could be measured, both before and after initiation of RRT, were selected for study.¹⁰ Three months after dialysis began, functional status had been maintained in approximately 40% of the cohort, but after one year, nearly six out of ten died, and pre-dialysis functional status was preserved in only 13%. It became clear that *dialysis itself* initiated a marked decline in functional status for these elderly nursing home residents. Theories as to why the decline occurred included various manifestations of depreciation and age-related decreases in reserve such as additional baseline disabilities and comorbidities correlated with aging (like heart failure), hospitalizations associated with renal failure and RRT, and aspects of the dialytic treatment itself (access issues and hypotension as two examples). The study was criticized because

there was no control group, that is, comorbidity-matched individuals who did not require dialysis.¹¹

Furthermore, some suggested aggressive rehabilitation might have arrested the observed decline, but it was not part of the design.^{12,13} In response, other investigators presented similar data.¹⁴ Applying regression analysis to estimated glomerular filtration rate for dialysis start time in ESRD persons 70 years of age and older, dialytic versus conservative therapies were compared in regard to survival. Although the dialysis cohort experienced longer survival, the additional time was at the expense of either hospital visits or interventions to maintain dialysis. The investigators noted that individuals in the dialysis group were approximately four times more likely to die in an acute hospital setting. A similar premise was studied in a geriatric cohort followed from 2000-2005.¹⁵ In this group, a majority of patients were living at home (76/90), not in extended care facilities, prior to initiating RRT. Nearly one-third of this cohort required Nursing Home placement after RRT was initiated. This study also suggested that dialysis per se had a profoundly negative health impact on this particular age group.

Most reviews on dialysis outcomes in elderly cohorts refer to a seminal study by Murtagh and colleagues. This study attempted to weigh comorbidity variables in elderly who required RRT.¹⁶ The study was retrospective and included 129 individuals older than 75 years of age who had renal functional impairments necessitating RRT. Patients were placed into two groups: those treated with dialysis (n= 52) and those choosing a conservative, non-dialytic approach (n= 77). Even though the number of individuals who qualified for ESRD and were simultaneously burdened with comorbidities, was small (n= 25; dialysis in 10, conservative approach in 15), mortality curves were superimposed, indicating dialysis did not provide medical benefit compared to conservative care. Other investigators, coming from a broad international background, have validated Murtagh's survival pattern in similarly comprised geriatric ESRD populations.¹⁷⁻²² In addition to ischemic heart disease as one critical comorbidity in ESRD elderly, other variables predicted increasing (but not invariable) six-month mortality.²² Dementia (a hazard ratio [HR] of 1.88) and peripheral vascular disease (HR 2.24) each contributed to an increased six-month risk of death. Estimates tested and corroborated in this study correctly predicted likelihood of dying in 87% of individuals enrolled. Another investigation focused on supportive care in a "conservative" (that is, non-RRT group who were in kidney failure) population.¹⁹ It explicitly practiced "maximum supportive care," characterized by pain control, erythropoietin, dietetics, etc., without explicit suggestions aimed at hastening death. This palliative approach was offered as a deliberate alternative to RRT.

Another Side to the RRT Coin: Age May Not Negatively Affect Transplantation

Transplantation is different than dialysis, especially with regard to the benefits accrued by the elderly. At this point in time (that is prior to possible rationing), the elderly are permitted access to transplants as expensive, scarce, non-renewable resources. However, the European model for allocation has applied age in a unique manner. The application of age has to be ethically contextualized. It represents neither medical benefit nor social valuation. Rather it accounts for expected life years after transplant.

Since 1999, the Eurotransplant Senior program (ESP)²³ has allocated kidneys from donors 65 years-of-age or older to similar age range recipients. As a result of ESP's success (i.e., obtaining more kidneys for the elderly on waiting lists by an expansion of the donor pool), the U.S. allocation agency, UNOS, is considering an allocation model similarly incorporating "Life Years from Transplant." Such a model utilizes age-related depreciation predictions for both donor and recipient.⁸ Put another way, since it is realistic to assume that an "average" 65-year-old transplant recipient will not live as long as a 25-year-old recipient, it may be prudent to try to match longer surviving kidneys (from younger donors) to younger recipients. In one study, the ESP group (1,406 individuals who received age-matched, "older" kidneys) was compared to cohorts receiving grafts from any age group (i.e., old donor to any age or any age donor to old recipient).^{24,25} The ESP model experienced an increase in the number of elderly donors (utilizing more marginal, older donor grafts that would have been previously discarded), a decrease in cold ischemia time, delayed graft function, with some increase in rejection rates. The downside of more frequent rejection and delayed graft function is important but not the entire story. The increase in elderly donors, consistent with greater acceptance of marginal donor grafts, may have a significant positive impact on elderly survival outcomes after transplantation rather than the opposite. It has been empirically proven that the elderly have increased survival after transplant when they receive a graft within two years of ESRD onset as opposed to waiting longer.⁷ So, an allocation scheme that increases grafts for the elderly, especially early on, could improve survival, as long as the grafts, though "marginal," remain viable. The ESP, implementing like-aged allocation, did *not* adversely affect graft and patient survivals overall. Although older patients receiving younger grafts had better overall survival compared to the older-older schema, the old-to-old model decreased waiting time for potential geriatric recipients by making more kidneys available. This earlier transplantation advantage may lead to better survival as both numbers and experience increase. Differences between dialysis and marginal graft transplants for this population have demonstrated an insignificant net difference in survival—a critical ethical point.

Unlike dialysis survival, elderly transplant schemes require further "ethical unpacking." The first observation would also be evaluative: social value criteria are not applied to exclude the elderly from organ access in Europe. However, physical depreciation is used to estimate overall survival or life years expected after transplant. Essentially, older transplant recipients do not live as long as their younger counterparts, itself an actuarial reality. Therefore, whatever negative effects marginal or older organs have on their recipients, the application of age-related depreciation formulas provided more organs and will eventually provide improved survival for the cohort compared to the prior waiting list.

In the United States, UNOS records were also searched for 47,535 adults receiving deceased donor kidneys (1995-2002).^{24,25} A "Recipient Risk Score" was derived, tabulating both graft and patient survival after transplant. The strongest predictors of recipient survival after transplant were age (not surprisingly), a history of diabetes, angina, and, again, duration of dialysis. The authors suggested that the lowest risk kidney grafts (from younger, healthier donors) be allocated to lowest risk patients (again, younger and healthier). If applied, it is predicted that the scheme would maximize years of potential graft function (apropos of "Life Years after Transplant" as with ESP), at the expense of actuarial depreciation consonant with aging. If the allocation rule had been in effect over

the duration of the study (as in Europe already), it would have purportedly increased the annual supply of transplantable kidneys for 2002 by 15%. This fact is not presented as a utilitarian calculus to merely serve the young cohort in the proposed equation. From an ethical perspective, such a methodology would represent social valuation and therefore would be unjust. Experience has demonstrated that organ supplies increase with that intervention, and earlier transplantation in the elderly provides a salutary impact on their survival. The negative features—that is, delayed graft function and some increase in rejection rates—do not cancel the survival benefits of earlier transplantation in a geriatric cohort. In this author’s opinion, as long as the elderly have free access to organs and obtain medical benefit, life years after transplant schemes are ethically acceptable.

From an economic perspective, because of the initial, front-loaded expense of a kidney transplant (for surgery, laboratory, drugs, and hospital stay), it takes approximately two years to recoup costs compared to dialyzing an individual without transplant. In the elderly, it may take closer to three years. After this interval, post transplant, “younger” transplant recipients save Medicare or third party payers approximately \$3,800 per month, the elderly save \$2,400.²⁶

Discussion

As the contrast between dialysis-RRT versus transplant-RRT has demonstrated, factoring age into access decisions can never be considered a “homogenous” (or one size fits all) approach. Although medical benefit criteria suggest that dialysis-RRT leads to functional deterioration in the elderly and may actually be no better than conservative care, the same negative appraisal does not hold for transplants. Therefore, attempts to factor age into future rationing decisions could be fraught with potentially unethical consequences. However, carefully considering medical benefit for all age groups—not only the elderly—does not discriminate through social valuation. This author suggests that the absence of medical benefit with dialysis in those older than 75 years with comorbidities should be considered in access decisions. As a corollary, elderly should not be barred from renal transplantation utilizing the same ethical model.

Would suggesting the elderly be relieved of the burden of specific therapies that do not obtain benefit (in this instance dialysis accompanied by comorbidities) have potential negative consequences? Although medical benefit criteria have been empirically applied to prove that RRT-dialysis provides little or no benefit to geriatric persons with ESRD (especially those individuals 75 years of age and older further burdened with comorbidities like heart failure), there are still a number of difficult problems in proposing any age-driven depreciation models. First, one segment of therapy (that is, RRT-dialysis) cannot be generalized to other therapies or organ systems without empiric study. In this manuscript, supportive data has been accumulated for only two treatment modalities affecting one subspecialty in medicine. The data presented are at best a simple answer to a remarkably complex problem. The U.S. census has determined that the U.S. healthcare “industry” contains 340,650 separate entities employing 5,508,926 individuals. Within these numbers, 512,000 physicians practice alongside 2.2 million nurses. The RRT data should not be extrapolated from a limited nephrology perspective to policies encompassing broader therapeutic contexts.

The “extrapolation claim” becomes evident if age is factored into renal transplant allocation decisions. Age alone does not predict compromised survival after transplant and is categorically different in this important regard than RRT-dialysis. It is not surprising that a geriatric population does not tolerate the rigors of three times weekly dialysis. Even though transplant surgery and immune suppression are hardly benign, they do not appear to be as “physiologically erosive” as RRT-dialysis. So, using age per se to limit transplantation access, or, for that matter other, unstudied expensive therapies, is social valuation and therefore wrong.

A second concern is that the difference between limiting access solely based on the criterion of age versus limiting selected therapies conferring negligible medical benefit may be difficult to conceptualize at a “grass roots” level. Recent history has demonstrated that healthcare reform requires the broadest consensus in order to achieve success. Would Americans be capable of differentiating medical benefit criteria from social value-laden decision-making? At the risk of being coined an elitist, one would answer “not likely.” If any confusion opens further inroads to access for the elderly, especially at a time when Medicare is bearing the brunt of payment, it would be unethical to proceed.

Evidence has been uncovering other therapies that provide negligible benefit—in these instances, across all age groups. One example may be bevacizumab, an expensive angiogenesis inhibitor used to treat metastatic cancer.^{27,28} Financial analysts predict sales of this single pharmaceutical may reach \$7 billion/year. On an individual level, bevacizumab adds one year of life to advanced cancer sufferers at a price tag of \$230,00 per patient for that one year. In other words, the drug extends life on average approximately a matter of months at a cost of \$50,000 for the time added. As a result, the British National Health and Excellence Service will not make bevacizumab available through its health plan. That group has made a specific access decision based on medical benefit, not age. If medical benefit will prosper in an ethical, just environment, it will have to be understood as age-neutral by consensus. An intervention that does not work should not be given to anyone, regardless of his or her age.

As difficult as access decisions will become, likely leading to consideration of rationing, there have been some interesting developments in response to dialogue engaging elderly RRT-dialysis. Educational agencies are suggesting increased attention to palliative care for nephrologists as a result of the aforementioned data. This approach is unique and demonstrates that healthcare professionals are realizing that medical benefit can be used to determine access and alleviate unnecessary and burdensome therapy. From a Christian perspective, the developments open a door to leadership and action in the realm of palliation. Attention to pain relief, “palliative dialysis, that is, concomitant palliative and hospice care for those elderly who choose to pursue dialysis, and understanding that palliative interventions actually prolong life not hasten death will be a welcome addition to U.S. medical care.”^{29,30,31}

Finally, the transplant data in the elderly must be presented in stark contrast to RRT-dialysis. Their juxtaposition is proof that age alone cannot be the criterion for medical access decisions. Although there is some ethical concern regarding age-to-age allocation schemes (rejection and delayed graft function), the model permits elderly access and seeks good outcomes for geriatric individuals.

Although it may be an emotionally trying time in medicine, medical benefit-cost appraisals should become a staple of the reform debate. They are ethically superior to a resuscitation of social value-laden decision-making. However, it is imperative while this portion of debate evolves that the ethical differences between access by age (social valuation) compared to access by medical benefit be clearly delineated. Since debate has been fractious, and since the elderly have become an “economic whipping” group, this may not be an easy task. Championing palliative care and eschewing death-hastening must accompany discussion.

The purpose of this paper was to study healthcare reform and suggest ethical alternatives to limiting care through to social valuation. Future debate may become grim, especially targeting the vulnerable among us. Medical benefit may be the only just way to respond to an expanding crisis.

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THE ETHICS OF OVARIAN TISSUE TRANSPLANTATION: A TELEOLOGICAL PERSPECTIVE

SISTER RENÉE MIRKES, OSF, PHD

Abstract

Many female patients present with malignant and non-malignant conditions whose treatment causes infertility. Women who are diagnosed with neoplastic diseases before¹ or during² their reproductive years and undergo ootoxic therapies,³ those who undergo an oophorectomy due to non-malignant disorders,⁴ those of reproductive age at risk for premature menopause associated with genetic disorders, and those who have undergone conditioning regimens for bone marrow transplantation⁵ may experience partial or total loss of their fertility.⁶ Fortunately, in recent decades, medical science has witnessed dramatic improvements in chemo-⁷ and radiotherapy⁸ for neoplastic diseases together with noteworthy advances in fertility preservation techniques. Such advances have allowed more and more women who survive malignant and non-malignant illnesses⁹ to focus on improving their post-treatment quality of life, including the restoration of their fertility and the possibility of childbearing. Ovarian tissue cryopreservation¹⁰ and transplantation,¹¹ though still experimental,¹² hold out real promise¹³ for these women.

Here, I will conduct a teleological analysis of selected ethical issues¹⁴ from three clinical cases of women who experienced the reactivation of ovarian function and a live birth as a result of ovarian tissue transplantation (OTT). In case #1, a woman who experienced ovarian failure after cancer therapy for non-Hodgkins lymphoma subsequently conceived by means of IVF following a frozen-thawed ovarian autograft. In case #2, an infertile monozygotic twin conceived spontaneously as a result of a fresh ovarian graft¹⁵ from her fertile identical twin, and, in case #3, a woman who experienced ovarian failure after cancer therapy for stage IV Hodgkins lymphoma conceived spontaneously through autotransplantation of frozen-thawed ovarian tissue. Lastly, I will assess the ethics of case #4 in which a healthy woman has stored her ovarian tissue to prolong her reproductive life.

Part One— Ovarian Tissue Transplantation: What's Involved?

A. Collection and Cryopreservation of the Ovarian Tissue

Because of the ootoxic nature of chemo- and radiation therapies, the goal is to harvest ovarian tissue before the woman undergoes these therapeutic regimens. Theoretically, there are three ways of cryopreserving ovarian tissue: as fragments of ovarian cortex,¹⁶ as a whole ovary with or without its vascular pedicle, or as isolated follicles.¹⁷ In current practice, however, OT cryopreservation (and transplantation) is almost exclusively limited to avascular fragments of the ovarian cortex.¹⁸ Most primordial follicles are contained in the outer layer of the ovarian cortex and, fortunately, are less susceptible to cryoinjury than more mature oocytes. In the collection process via laparoscopy or

laparotomy, then, surgeons remove the millimeter-thick outer shell of the ovary, cut the cortex into strips around 1-3 mm in thickness and up to 1 cm² in total area, and allow the cryoprotectants to thoroughly penetrate the tissue. Each of these strips potentially contains thousands of primordial follicles capable of developing into mature oocytes or egg cells when thawed and transplanted.¹⁹ A slow-cooling technique was originally used to freeze the excised ovarian tissue. More recently, however, vitrification—a fast-cooling method of cryopreservation—has proven effective in reducing cryoinjury due to formation of ice crystals.²⁰

Before being frozen, however, each cortical strip must be examined both for the presence of primordial follicles and the absence of malignant cells. One of the primary risk factors of cryopreserving ovarian tissue from cancer survivors and, *a fortiori*, a critical ethical issue for those researchers who are experts in OTT and responsible for its ongoing refinement, is that of re-implanting malignant cells through the graft. For this reason, then, research clinicians insist that, prior to any cryopreservation of ovarian tissue, strict IRB oversight of OTT²¹ must require thorough examination of ovarian graft tissue to verify the absence of neoplastic cells.

B. Transplantation of the Ovarian Tissue

Only after the woman survives the therapeutic regimen that treated her disease, is declared disease-free, and is fit enough to request the replacement of her ovarian tissue for reproductive purposes will the surgeon thaw and then replace the cryopreserved tissue. The transplantation of ovarian tissue has been successfully attempted with various tissue sizes from cortical strips to the whole ovary either with or without the vascular pedicle. Typically, transplantation of fresh ovarian tissue would include a variety of tissue sizes, while transplantation of previously frozen ovarian tissue only uses cortical strips.

Ovarian tissue can be grafted orthotopically or heterotopically. Orthotopic transplantation involves the transfer of fresh or cryopreserved ovarian tissue to the ovary itself or the area surrounding the ovary: the peritoneum of the ovarian fossa, and/or to the remaining ovary.²² It is important to note that natural or spontaneous conception in the context of OTT can only take place with an orthotopic graft. To date, all the reported live births following OTT have resulted from orthotopically transplanted ovarian grafts.

Heterotopic transplantation involves the transfer of fresh or frozen ovarian tissue to locations outside the ovarian region: the arm, the forearm, the rectus abdominis muscle, and the subcutaneous tissue of the abdominal wall. Minimally invasive and providing easy access to mature eggs, ovarian tissue transplant to the abdominal wall or forearm is the heterotopic site of choice. Transplanting ovarian tissue heterotopically is easier and less risky than an orthotopic graft and allows easier monitoring of follicular growth.²³ Nonetheless, heterotopic transplantation necessitates IVF-assistance should the woman pursue conception.²⁴ Fertility researchers have proven that oocytes can be aspirated from heterotopically-grafted ovarian tissue, matured *in vitro*, and used for IVF-assisted pregnancy.²⁵ In some cases, both orthotopic and heterotopic grafts are combined in hopes that the heterotopic tissue will stimulate the orthotopic graft to produce ovarian hormones and mature oocytes more efficiently, thereby facilitating natural conception.²⁶

Some fertility researchers report that, following the freeze-thaw process, primordial follicles are able to tolerate ischemia for at least four hours.²⁷ Transplantation of strips of ovarian cortex is done without vascular reanastomosis. Hence, the health of the

graft depends on the growth of new blood vessels, and the vigor of ovarian function depends on a good blood supply to the ovarian graft. A newer, two-part transplantation technique appears to have resolved the problem of reducing the length of time between transplantation and neovascularisation²⁸ to avoid ischemic follicle depletion and loss of function and quality in the ovarian graft. Surgeons graft small pieces of cryopreserved ovarian tissue in the ovarian and peritoneal areas three days before the actual ovarian tissue transplant. The first graft increases the blood flow to the ovary by encouraging the graft to recruit its own blood supply via newly grown blood vessels, facilitating its principal goal: to make the ovaries more responsive to the action of hormones that induce them to release eggs each month.

C. Possible Reproductive Outcomes

Most often, transplantation of ovarian tissue has two goals: to restore hormone production and to facilitate follicular development in order to achieve pregnancy. A 2007 survey²⁹ of reproductive outcomes of OTT reported that the transplantation of ovarian tissue did establish ovarian function after premature ovarian failure (POF). In a review of 46 unique cases,³⁰ OTT was used to treat POF in 27 women, to prevent POF in 15, to treat infertility in 2 and accidentally in 1. For 23 women in POF at the time of OTT, ovarian function was restored. After six months of ovarian restoration, however, four women experienced recurrent ovarian failure. Women receiving fresh grafts showed an increased likelihood for the return of their ovarian function and a decreased likelihood for recurrent ovarian failure. Insufficient data disallow evaluation of long-term (>12 mos) ovarian function. Of the 27 women who underwent an OTT, 25 sought pregnancy. Eight of these achieved nine pregnancies for a 12-month cumulative pregnancy rate of 37%. Four of the eight women who conceived had frozen-thawed ovarian grafts and four had fresh grafts. Five women achieved pregnancy spontaneously; three women got pregnant via IVF and embryo transfer. By the close of the survey period (June 2007), three of the pregnant women had given birth to full-term babies, and four women still had ongoing pregnancies. Two of these deliveries followed the autotransplantation of frozen-thawed ovarian tissue and the third was after heterologous transplantation of fresh cortical tissue between twin^s discordant for POF. As of 2009,³¹ the orthotopic autotransplantation of cryopreserved ovarian tissue had resulted in the birth of five healthy babies worldwide.

Part Two— Ethics Analysis: From a Teleological Perspective

My approach to adjudicating the ethics of OTT—that of a teleological prudential personalism³²—represents a middle course between a pragmatic and deontological ethics, between, on the one hand, those who solve ethical problems based less on principle and more on emotion or on subjective pragmatism and, on the other, those who adjudicate moral issues based on obedience to absolute principles or authoritative laws. As such, my analysis of the ethics of OTT in its varied applications is *personalist* and *teleological*. It is based, first, on an *a posteriori*, realistic understanding of (1) the basic needs/goals of the human person and human nature that comes from empirical induction and (2) the human fulfillment (personal and communal) that is derived from the realization of these needs.

When you or I think about ourselves or observe other human persons informally—or academically within the life and social sciences—two contrasting facts about humans

stand out. Though an individual, each of us is at the same time someone who exists “with” and “for” another and someone who finds fulfillment not in solitude but in communion with others, in an ever-expanding set of communities. We recognize that while each of us is unique, each person is also a member of the same species, *homo sapiens*; each of us lives in one global human community and strives for the same goals, goals that can only be reached by common action. In other words, empirical observation helps us see that every person is a “dynamic system of needs” and, as such, is teleologically defined by these basic needs or goals in their hierarchy: to preserve life, to procreate, to live in society, and to know the truth. So, from conception forward, every human person has physical needs for safety and security as well as nourishment and health that are the primary means for satisfying other, “higher” needs. These needs are higher in the sense of being spiritual needs, needs that make it possible for human beings to transcend the goals they share with plants and animals. So, our empirical study of human nature advises us that every human person needs a good family life, needs the truth of reason and of faith that leads to sound self-understanding—who we are and for what or for whom we are made—needs to know and love others, and, preeminently, needs to know and love God.

Based on both empirical and existential experience, we also conclude that what constitutes a reasonable system of ethics or moral human behavior is for human persons to satisfy these basic needs and the needs of others in a harmonious way, both in their order of necessity and in their order of importance. Acting consistently to realize their basic needs in themselves and in others leads human beings to an integrated *ethos* of happiness: the goods of life, health, security, and human dignity; the good of a personalized sexuality, a loving family, and society; the good of true self-knowledge and wisdom. In short, when you and I fulfill our basic human needs in their order of importance, we are ethical persons—naturally fulfilled and happy. Conversely, when you and I freely act in ways that abuse, destroy, or thwart our basic needs, we act against our basic personal and communitarian goods/values that comprise human flourishing. Or, to state it differently, when we arrest or circumvent our basic human goals, we act irrationally, failing to realize integral human fulfillment in a free and intelligent way.

Second, my personalist and teleological analysis is based on moral principles that, *a priori*, arise from knowledge of these basic human needs (every human being needs to preserve life, to procreate, to live in society, and to know the truth) and expatiate their content. Personalist principles are, therefore, capable of guiding people to intelligently analyze the ethics dimensions of concrete situations and to help them realize integral human fulfillment both individually and culturally through consistently choosing personal and communal good in their actions. Two personalist moral principles, pertinent to the OTT cases I analyze here, will illustrate my point.

Based on the basic human need to procreate (and the correlative goods of sexuality and offspring), we can formulate the principles of (a) personalized sexuality and (b) family-oriented sexuality:

- (a) We, like higher animals, reproduce and raise our offspring sexually. Just as our need to eat is supported by physical pleasure, so is our need to procreate. But, for human persons, the need to propagate the human species is also achieved by sexual acts of intercourse that are expressive of a personal union of committed love between husband and wife and of mutual love for their offspring.³³

(b) The gift of human sexuality must be used in marriage in keeping with its intrinsic, indivisible, specifically human teleology. It should be a loving, bodily, pleasurable expression of the complementary, permanent self-giving of a man and woman to each other which is open to the perpetuation and expansion of this personal communion through the family they responsibly beget and educate.³⁴

My ethical assessment of OTT, then, will not be focused on whether those who choose to access this reproductive technique are doing so out of obedience to rules or emotivist urgings or to realize the greatest good for the greatest number or any other consequentialist goals. I will adjudicate this fertility preservation technique *prudentially*, that is to say, using personalist principles to wisely discern whether OTT, in the four settings analyzed here, promotes a personal and communitarian ethics of authentic love. The principal adjudicative question I ask is this: Would a woman, choosing to access OTT in these various applications, realize her full human personhood and the happiness of her spouse and child?³⁵

*Case #1: IVF Conception and Live Birth Following Ovarian Autotransplant*³⁶

In some centers, all of the women entering the OTT study are offered assisted reproductive services (IVF) to increase their chances at conception, since the lifespan and quality of the grafts were largely unknown.³⁷ At the Chaim Sheba Medical Center in Tel Hashomer, Israel, Dror Meirou and his colleagues reported a live birth after IVF,

following the transplantation of thawed cryopreserved ovarian cortical tissue into the ovaries of a 28-year-old woman who had ovarian failure after high-dose chemotherapy for non-Hodgkin's lymphoma. Ovarian tissue (containing many primordial follicles) was harvested after administration of a second-line conventional chemotherapy regimen, before treatment with high-dose chemotherapy. The patient's menses ceased after the high-dose chemotherapy. During the ensuing 24 months, the amenorrhea persisted and laboratory testing consistently revealed high levels of follicle-stimulating hormone and luteinizing hormone and undetectable levels of anti-müllerian hormone and inhibin B—findings consistent with ovarian failure.

At 24 months post-treatment, the woman requested reimplantation of her cryopreserved ovarian tissue in order to restore her fertility. With approval from the institutional review board³⁸ and with her informed consent, the patient underwent a laparotomy during which strips of her thawed ovarian tissue were transplanted to the left ovary and small fragments were injected into the right ovary. Only the ovarian strips in the left ovary resumed function.³⁹ Eight months post-transplantation, the patient menstruated spontaneously. Basal levels of antimüllerian hormone were found in concentrations consistent with early-stage developing follicles. Then a rise in inhibin B levels characteristic of ovulatory women was identified. An ultrasound study showed a preovulatory follicle in the left ovary. Nine months post-autotransplantation, the patient had a second spontaneous menstrual period. IVF was performed; a single mature egg was collected (via transvaginal follicle aspiration) and fertilized in vitro with her husband's sperm. Two days later, a 4-cell embryonic human being was transferred to the mother's uterus. Repeated ultrasonography showed a normal pregnancy, and at 38 weeks 5 days of gestation, the patient delivered a healthy-appearing female infant.

Case #1: Ethics Analysis

Any female patient who experiences iatrogenic loss of fertility needs to preserve her life by pursuing good health. In this case, that need is satisfied through the OTT procedure—up to a point. Certainly, the collection⁴⁰ and cryopreservation of her ovarian tissue fulfills that need since healing—the restoration of her fertility—was the intent of those initial steps. But, with the patient’s (informed) consent to transplant her ovarian tissue heterotopically, she necessarily limited herself and her husband⁴¹ to an IVF-assisted conception (predicated, of course, on the success of the graft, i.e., on whether it restored ovarian function and produced oocytes capable of being used *in vitro*). In the technological act of producing their child with the assistance of IVF, the woman and her husband forfeited a nexus of basic human goods. Specifically, they frustrated their need for a sound self-understanding, for responsible self-determination, for integral fulfillment as parents, and for a family life in which the child learns the meaning of true love from their parents’ life-giving love—all values that follow directly from the satisfaction of the need to procreate in a truly prudential way.

Is such a sweeping indictment defensible, you ask? Yes, and for very cogent personalist reasons. In the first place, the patient and her husband were deprived of the (good of) knowledge that comes from discovering and respecting the laws of their sexual nature, especially the principle of the radical interdependence between the unitive and procreative dimensions of their sex acts. Knowledge of this truth—that having babies demands, activates, and defines the couple’s act of sexual union—would have helped the couple make sense of the mystery of their sexuality and the transcendent drama of their commendable desire for a child. Deprived of this wisdom—the good of conceiving a child within the only context worthy of human dignity—the patient and her husband were depersonalized, reduced to by-standers of, and suppliers of, fertilization material for a sterile laboratory procedure in which strangers presided over the genesis of their child.

Second, instead of benefiting from the important psychological good of being the personification of his parents’ love—connected to the protection, security, and, yes, intimacy of their bodily union—the child is reduced to an end-product controlled by scientific technology. The child, just as tragically as his parents, is also depersonalized and objectified.

Third, by pursuing an IVF-assisted pregnancy, the patient and her husband are denied the familial good of knowing each other—as mother and father—in their child who is conceived within their act of love, and the child is deprived of knowing himself as a beloved son or daughter in and through his parents’ bodily act of mutual self-gifting.

And, fourth, the patient’s choice of IVF placed the child’s basic need to preserve his life at great risk. What if, at her embryonic stage and before being transferred to her mother’s uterus, the child had been found to be genetically or chromosomally abnormal and either disposed of immediately or donated to destructive embryonic stem cell research? Or, what if she were tagged as a “spare” or “extra” embryo and relegated to the surrealistic suspension of cryopreservation?

Thus, for all these reasons, the answer to the question posed initially—Would a woman, choosing to access OTT to achieve an IVF-assisted pregnancy, realize her personal happiness and that of their spouse and child?—is in the negative.

Case #2: Spontaneous Conception in an Infertile Monozygotic Twin Following Ovarian Transplant from the Fertile Twin

The OTT procedure between monozygotic twins discordant for fertility (one twin was fertile, the other was prematurely infertile) was conducted by Dr. Sherman Silber and his colleagues after approval from the ethics review committee of St. Luke's Hospital and after informed consent from both women. Prior to the collection of ovarian tissue, both women were screened for hepatitis B and C viruses, and, two weeks before surgery, the recipient twin was taken off the oral contraceptives intended as hormone-replacement therapy. The surgeon removed the donor twin's left ovary under general anesthesia, and then dissected it, on ice, into strips 1 to 2 mm in thickness.

Meanwhile, the recipient underwent a minilaparotomy through a 3.5-cm incision above the pubis. The cortex of each streak ovary was resected . . . exposing the entire raw surface of the medulla. No follicles were observed. Hemostasis was meticulously controlled in the medulla . . . and continuous irrigation with heparin-treated saline in order to prevent the formation of a hematoma under the graft, but at the same time care was taken to avoid impairing revascularization by minimizing the amount of cautery. A section of approximately one third of the donor ovarian cortex was laid over the raw medulla of each ovary in the recipient and sutured onto the medulla The remaining third of the donor ovarian cortex was cryopreserved after equilibration . . . and slow cooled in an automated freezer. Tissue from the ovaries of both women were fixed in Bouin's fluid for histologic examination.

Seventy-one days post-transplantation, the development of a mature follicle, the presence of estradiol, levels and a proliferative uterus signaled that ovulation had occurred. At eighty days, the woman had her first postoperative menses, lasting one day. Her ovaries then remained quiescent until 48 days later when another mature follicle was found sonographically. At 141 days post-transplant, the recipient twin's FSH and LH levels had decreased to post-ovulatory levels and a second heavy period ensued.

On day 176 post-transplant (five weeks after her second menstrual cycle), an ultrasound study revealed a normal intrauterine pregnancy that occurred spontaneously. At seven weeks, an ultrasound showed a normally developing intrauterine pregnancy, and at 22 weeks another ultrasound showed the baby was developing normally. At 38 weeks gestation, the recipient twin vaginally delivered a healthy baby girl.

Case #2: Ethics Analysis

It is true that the woman in this study chose OTT to fulfill her basic need to procreate, but, examining the outcomes of using OTT in the context of a syngeneic graft, we see such a choice sabotages rather than realizes the procreative good. More, the choice thwarts some of the recipient twin's basic sexual, psychological, and familial needs and those of her husband and child. For although the donated graft made the recipient fertile, it was not really *her* fertility that was restored; although the ovarian graft allowed the recipient to achieve a pregnancy, it wasn't really *her* biological child who was conceived. Although the recipient twin conceived the child within an act of sex between her and her husband, it was not a genuine act of complete reciprocal self-gift of their sexual bodies since it included her sister's eggs rather than the gift of *her* oocytes. And although the

graft recipient brought a healthy baby to term, the biological reality is that her sister is the baby's genetic mother.

Thus, although the patient's husband could know and understand himself as father in and through the baby, the patient could not come to the correlative knowledge of her motherhood through the baby. And as the baby matures and begins to reflect on her own conception, I would predict she will seek out her biological mother (her aunt) in much the same way adopted children do, feeling the need to be connected somehow to the biological mother and father whose genomic self-gift they personify.

And, with a tragic irony, since the choice of OTT for monozygotic twins discordant for fertility necessarily involves imprudent actions from both twins, the personal and communal harm experienced by the infertile twin is duplicated in the personal and familial life of the fertile twin. And, since a healthy society is inextricably linked to the well-being of the basic cell of the family, the choice of OTT for monozygotic twins discordant for fertility, *a fortiori*, injures the larger society and culture as well. In sum, a woman who would choose OTT under these circumstances would realize neither her personal fulfillment nor the comprehensive happiness of her spouse, her child, and her twin sister.

Case #3: Spontaneous Conception and Live Birth Following Ovarian Autotransplantation⁴²

In 1995, the ethics committee of the Catholic University of Louvain approved a protocol to examine the safety and efficacy of the cryopreservation of ovarian tissue for women who were in treatment-induced ovarian failure as a result of high doses of chemotherapy.

In 1997, a woman with stage IV Hodgkin's lymphoma presented at the Catholic University's Gynecology Research Unit. After obtaining her informed consent, researchers collected five biopsy samples laparoscopically—each about 12-15 mm long and 5 mm wide—from the left ovary. The surgeons cut four biopsy samples of ovarian cortex into 70 small cubes of 2X2 mm, and one strip of 12X4 mm was left whole. All ovarian fragments were suspended in a cryoprotective medium, placed into precooled cryogenic vials filled with a Leibovitz medium, cooled in a programmable freezer, and eventually transferred to liquid nitrogen. Following the laparoscopy, the patient underwent hybrid chemotherapy and was amenorrheic shortly after initiation of the chemo. After chemo- and radiation therapy, the patient's FSH, LH, and estradiol levels all confirmed castration, and POF was confirmed three months later. In June of 1998, the woman was given hormone replacement therapy and then stopped in 2001, since she wanted to achieve a pregnancy. After a thorough examination, she was declared cancer-free. The surgeons did the first laparoscopy seven days before reimplantation to create a peritoneal window in order to induce angiogenesis and neovascularisation in the area. Although there was a small corpus luteum on the left ovary, the patient's LH and FSH returned to castration levels.

Surgeons then did a second laparoscopy seven days later and removed a biopsy sample, 4-5 mm in size, from both ovaries which was cryopreserved, thawed, and immediately transferred to the operating theater.

We pushed the large strip and 35 small cubes of frozen-thawed ovarian tissue into the furrow created by the peritoneal window very close to the ovarian vessels

and fimbria on the right side. No suture was used. An extensive neovascular network was clearly visible in this space. We used vital fluorescent staining to confirm survival of primordial follicles after freeze-thawing.⁴³

After prolonged discussion between oncologists and the patient, surgeons performed a third laparoscopy to check the viability of the grafts, to insure the absence of malignant cells, and to reimplant the remaining ovarian cortical cubes. At the site of reimplantation, the follicular structure that was previously identified at vaginal echography was seen and biopsied. The grafted cubes were also biopsied and checked for follicle survival. The remaining 32 ovarian cubes were transplanted on the right side and a slight reduction in LH and FSH was recorded, consistent with follicular development in the grafted area. Five to nine months after reimplantation, ultrasonography revealed a mature follicle and a corpus luteum. This began restoration of consecutive monthly menstrual bleeding. At 9.5 months after reimplantation, FSH concentrations peaked and then returned to normal levels 7 days later. After three weeks, a ripe follicle appeared “clearly outside the right ovary,” while both native ovaries were well visualized and “obviously atrophic.” From this ovulation, the patient conceived spontaneously. Eighteen days post-ovulation, a clinical pregnancy was confirmed through human chorionic gonadotropin concentrations and vaginal echography. Vaginal ultrasonography confirmed a viable intrauterine pregnancy 8 weeks later. At term, the woman gave birth to a healthy girl.

Case # 3: Ethics Analysis

Any woman who, as the female patient in this case did, chooses an orthotopic ovarian graft in hopes of restoring her fertility and achieving a pregnancy would also satisfy her need for health and survival, procreation, married friendship, family, and society in an integrally fulfilling way, both personally and interpersonally. By that I mean, the woman could reap the same concomitant human goods as did the female patient of this fourth case did. She would benefit from sound knowledge about the truth of personalized sexuality and the demands arising from the dignity of human procreation, reproductive health, a child conceived within a loving act of interpersonal union between wife and husband, a sturdy family built on the familial truth of the interpersonally-generated knowledge of what it means to be a loving parent and a beloved child, and a society which flourishes in a way commensurate with the strength and health of each family. In sum, then, were any woman to choose OTT under the circumstances described in this third case, she would not only help to realize her own personal fulfillment but would also take an important first step to promote the wholesome development of her spouse, her child, and the society at large.

Case #4: The Removal and Cryopreservation of Ovarian Tissue from a Healthy Woman to Postpone Childbirth

The *Wall Street Journal* reports⁴⁴ that the Infertility Clinic of St. Louis is one of the few or perhaps the only fertility center in the U.S. that performs cryopreservation of ovarian tissue for healthy women wanting to postpone pregnancy. The center’s director, Dr. Sherman Silber, is a pioneer in OTT and believes the technique ought also to be made available for healthy women. The procedure will work well, Silber insists, if women freeze their tissue in their 20s or 30s rather than waiting until their late 30s or 40s to do so. The goal of the St. Louis Center in making the cryopreservation of ovarian tissue

available for healthy women is to give these patients the reproductive advantage of transplanting their own youthful eggs when they are older.

A healthy patient in her early 30s underwent elective surgery at the St. Louis Center to collect her ovarian tissue, to cryopreserve it, and to re-transplant it in the event she had “a hard time getting pregnant in the future when she might be too old.” Source? The patient wanted to postpone pregnancy until after her husband secured his degree and earned a tenured university teaching position. Subsequent to removal and cryopreservation of her ovarian tissue, this patient conceived spontaneously, i.e., without help from her frozen reserves. Nevertheless, she confesses she is grateful that she made the decision to bank her tissue should she have needed the graft to help her overcome difficulty in conceiving the next time.

Case #4: Ethics Analysis

The *Wall Street Journal* interviewed Dr. Silber about his highly disputed promotion of OTT for healthy women. Defending his program, Silber argued:

What is the difference between losing your fertility from aging of your ovary or from cancer treatment? Either way you are losing your fertility, and freezing either your eggs or your ovarian tissue can preserve that fertility.⁴⁵

My response to Silber speaks to the way I would evaluate any case of a healthy woman who chooses OTT to prolong fertility into her late reproductive (or even menopausal) years, as did the woman in case #4. I strongly disagree with Silber’s egalitarian view that a healthy woman’s choice of OTT is the same as that of a woman with the iatrogenic loss of her fertility. The two cases—treatment-induced sterility of young women in their 20s and 30s and the natural waning of fertility in women in their mid-30s, 40s, and 50s—have distinct existential and ethical profiles. The loss of fertility in a reproductive-age woman represents a health deficit which she needs to restore in order to regain not only procreative but also systemic health. But a woman’s natural loss of fertility in mid-life, when she is heading toward retirement and her “senior” years, is a built-in (natural) protection against harm both to the woman and to possible children she might bear. From a health perspective alone, women in their late 40s and early 50s, short on optimal health, stamina, and energy, are more susceptible to pregnancy complications. From a sensible child-rearing perspective, is it fair to submit the child of elementary age to the predictable taunts of his classmates because his mother looks more like the child’s grandmother than mother? Is it fair to require the involved father to measure up to the challenging spiritual and physical demands of fathering that are routinely and logically required of younger dads? And is it fair to the larger society to weaken the family, its basic building block, because children are more likely to lose their parent or parents at an age when they still, or perhaps most, need their presence? To use cryopreservation of ovarian tissue to facilitate the deliberate postponement of childbirth and child-rearing until the twilight years of reproductive health, best of motives notwithstanding, is imprudent, unreasonable, and, therefore, unethical. But it is ethical to reverse, by moral means, the iatrogenic loss of fertility.

Other ethicists⁴⁶ argue that a woman’s right to reproduce in whatever way she likes at whatever time she likes trumps any objections to the use of OTT by healthy women that “appeal to nature.” They argue that the reaction that “nature’s boundaries are there

to be respected, not transgressed” and the familiar claim of popular-press reports that fertility preservation techniques such as OTT are ““playing God”” or ““tinkering with nature”” do not make “convincing moral arguments.”⁴⁷ But the natural law or prudential personalism that I appeal to here is not a matter of boundaries or limits but of our natural human needs for food, health, friends, and truth. If we fail to meet these needs in their order of importance, we simply cannot be happy (as in fulfilled) and we will not be acting ethically. These natural needs and the principles derived from them are the bottom line for assessing the morality of OTT or of any other concrete choices of life.

In sum, then, any healthy woman who would choose OTT to prolong ovarian function in the waning years of her fertility would not only thwart her own personal fulfillment but also would threaten the wholesome development of her spouse, any child she might conceive, and the society at large.

Conclusion

Of the four cases examined here, only the circumstances of the third case—spontaneous conception and live birth following ovarian autotransplantation—prove to promote a personal and communitarian ethics of authentic love by helping the woman who chooses it realize not only her full human personhood but the happiness of her spouse and child.

Endnotes

- 1 A. J. Jakumiuk and W. Grzybowski report that one in 600 girls will develop cancer (mostly leukemia, central nervous system, embryonal, lymphoma, and soft tissue or bone cancers). The life expectancy of young women battling these diseases has been so dramatically improved that they and their treating physicians expect a 90% chance of being cured. These statistics raise another ethics issue beyond the scope of this paper: the need to discuss fertility preservation options with prepubertal girls as well as with younger and older women facing iatrogenic loss of fertility *pre-therapy*, since restoration of reproductive capacity is important for their psychophysical well-being post-therapy [“Ovarian tissue preservation, present and clinical perspectives,” 32 *Gynecological Endocrinology* 2(2007):87].
- 2 OTT is also indicated for women in their thirties who will be treated for breast, ovary, uterine or cervix cancer, for oophorectomy due to non-malignant disorders (cf. fnnt 4), or for autoimmune diseases requiring gonadotoxic therapy [Jakumiuk, “Ovarian tissue preservation,” 90].
- 3 Ovaries are very sensitive to cytotoxic treatment and are at different levels of risk for premature ovarian failure (POF) from alkylating agents and from radiotherapy, depending on doses, irradiation schedule, and patient’s age when starting radiation [Ibid, 88].
- 4 OTT is suggested for women with non-malignant diseases: (1) those who have undergone uni/bilateral oophorectomy after presenting with a benign ovarian tumor, severe and recurrent endometriosis, BRCA-1 or BRCA-2 mutation carriers, (2) women at risk of premature menopause in the case of Turner’s syndrome, family history, or from benign diseases requiring chemotherapy: autoimmune diseases such as systemic lupus, rheumatoid arthritis, Behcet’s disease and Wegener’s disease and (3) women who undergo a bone marrow transplant because of benign hematological diseases such as sickle-cell anemia, thalassemia major and aplastic anemia, or autoimmune disease unresponsive to immunosuppression. [J. Donnez et al., “Ovarian tissue cryopreservation and transplantation: a review,” 12 *Human Reproduction Update* 5(2006):521].
- 5 The conditioning regimen for bone marrow transplantation represents “the most gonadotoxic regimen with an ovarian failure rate after treatment exceeding 90% (I. Demesteere et al., “Orthotopic and heterotopic ovarian tissue transplantation,” *Human Reproduction Update* (Advance Access published May 27), (2009):2). Hematopoietic stem cell transplantation (peripheral blood or BMT) have been used increasingly in recent decades for non-cancerous diseases such as benign hematological disease (sickle cell anemia, thalassemia major and

- aplastic anemia) and for women suffering from autoimmune diseases previously unresponsive to immunosuppressive therapy (systemic lupus erythematosus and autoimmune thrombocytopenia) [Donnez, "Ovarian tissue cryopreservation," 521].
- 6 Jakimiuk, "Ovarian tissue preservation," 87-88.
 - 7 Chemotherapy with alkylating agents that involve high risk of sterility for the female patient include cyclophosphamide, busulfan, melphalan, chlorambucil, dacarbazine, procarbazine, ifosfamide, thiotopa and nitrogen mustard; women are at medium risk from alkylating-like agents cisplatin and carboplatin and at low risk for gonadal dysfunction from methotrexate, bleomycin, 5-fluorouracil, actinomycin-D, mercaptopurine, and vincristine. "The type and doses of chemotherapeutic agents influence the progression to ovarian failure with alkylating agents increasing the risk of POF by a factor of 9. . . . Larsen et al reported a four-fold increased risk of premature ovarian failure (POF) in teenagers treated for cancer, and a risk increased by a factor of 27 in women between 21 and 25 years of age. . . . It is thus obvious that high doses of alkylating agents, irradiation and advancing age increase the risk of gonadal damage." (Donnez, "Ovarian tissue transplantation," 519). Demesteere et al. report that premenopausal women treated with alkylating agents have a 68% risk for POF ("Orthotopic and heterotopic," 2).
 - 8 "The effective sterilizing [radiation] dose is a dose of fractionated radiotherapy (Gray [Gy]) that causes POF immediately after treatment in 97.5% of cases. . . . For younger women and children it is likely that a total dose of 20 Gy over six weeks would produce permanent sterility, with 95% confidence. In women aged 40 years it has been shown that a permanent menopause may be induced by 6 Gy" [Jakimiuk, "Ovarian tissue transplantation," 88].
 - 9 By the year 2010, approximately one in every 250 people in the adult population will be childhood cancer survivors [Donnez et al., "Ovarian tissue cryopreservation," 519; Jakimiuk, "Ovarian tissue preservation," 87]. Presuming half of these survivors are women, the possibility of using OTT after sterilizing treatment to restore fertility would be a welcome option for a sizeable number.
 - 10 Cryopreservation, the process of preserving and storing living systems in a viable condition at low temperatures for future use, is accomplished, prior to the transplantation of the ovarian graft, using two different techniques: slow-cooling (older method, less effective) and fast-cooling or bitrification (newer method, more effective). Cf. *fn* 20.
 - 11 Jakimiuk, "Ovarian tissue preservation," 89.
 - 12 The Ethics Committee of the American Society for Reproductive Medicine recommends that the OTT procedure only be done in specialty centers and under IRB oversight and approval [83 *Fertility and Sterility* 6(2005):1622]. Women who are candidates for fertility preservation techniques need to be counseled about the availability of OTT and its experimental nature so they can properly weigh benefits against risks in giving their informed consent. For the sake of informed consent for these women and for those who will opt for OTT after it is introduced into mainstream clinical practice, future research by OTT experts needs to optimize the freeze-thaw process, resolve the difficulty of transient graft ischemia, and perfect the tests to detect cancer cells in the transplanted tissue (multiple biopsies submitted to thorough histological examination: molecular genetic techniques: polymerase chain reaction, flow cytometry, fluorescence in situ hybridization and cytogenetics) [Jakimiuk et al., "Ovarian tissue preservation," 87, 90-91]. In addition, Mohamed A. Bedaiwy et al. call for a "multicenter controlled clinical trial with sufficient follow-up (5 years) to systematically evaluate the efficacy of this procedure before wide clinical utilization" ["Reproductive outcome after transplantation of ovarian tissue: a systematic review," 23 *Human Reproduction*, 12(2008):2716].
 - 13 The Ethics Committee of the American Society for Reproductive Medicine reports that the only established method of fertility preservation, embryo cryopreservation, requires that the female patient who suffers iatrogenic infertility be of reproductive age, have a partner or use donor sperm, and be capable of a cycle of ovarian stimulation (which of course is impossible when hyperstimulation is contraindicated in certain types of cancer) and able to put off chemo- or radiological therapy long enough to go through the IVF process of producing embryos. Furthermore, another fertility preservation technique, oocyte cryopreservation, which could be performed in single women, has proved ineffective with pregnancy and delivery rates ranging from 1% to 5% per frozen oocytes. Thus, for prepubertal women and for cancer patients who

- must have chemo or radiation immediately, OTT is an attractive alternative to embryo or oocyte cryopreservation (Donnez, "Ovarian tissue cryopreservation," 519).
- 14 Ethical issues that are important but will not be considered here include the following: ovary donation from cadavers or fetuses to be used as xenografts or heterogeneic grafts for infertile women who elect OTT as a way to achieve pregnancy, how informed consent protocols for prepubertal girls scheduled to undergo sterilizing treatment should be conducted (with or without the patient's consent/with or without parental presence and advice), the legal protocol that needs to be in place to insure proper disposition of banked ovarian tissue should the patient not survive treatment, the use of pre-implantation genetic diagnosis (PGD) to screen oocytes for inheritable conditions in the context of OTT with an IVF-assisted pregnancy, and whether refusing OTT for healthy women is gender-discriminatory by denying women the fertility extension that men enjoy.
 - 15 The technical term for a transplantation in which donor and recipient are identical twins is syngeneic transplantation.
 - 16 The ovarian cortex consists of ovarian follicles and stroma in between them. Included in the follicles are the cumulus oophorus, membrana granulosa (and the granulose cells inside it), corona radiata, zona pellucida, and primary oocyte. The corpus luteum from the follicles is also contained in the ovarian cortex. [Helga Fritsch and Wolfgang Kuehnel, *Color atlas of human anatomy*, Vol II: *Internal organs* (Stuttgart, Germany: Thieme Verlag, 2005), p. 270.]
 - 17 Primordial follicles within the ovarian cortex or isolated are less susceptible to cryoinjury because they have "a relatively inactive metabolism, as well as a lack of meiotic spindle, zona pellucida and cortical granules. The small size of primordial follicles also greatly facilitates penetration of cryoprotectant. In 1997, Oktay and his colleagues (Fertility Preservation Program, Department of Obstetrics and Gynecology, Weill Medical College of Cornell University) "developed an isolation technique for human primordial follicles using enzymatic digestion and microdissection and obtained high follicular viability rates with both fresh and frozen ovarian tissues." Nevertheless, Donnez et al. argue that the procedure of isolating primordial (ovarian) follicles "remains difficult" ["Ovarian tissue cryopreservation," 528].
 - 18 *Ibid.*, 521.
 - 19 In the ovaries, there is a continuous process whereby eggs (oocytes) are constantly being prepared for the maturation process. After menarche, it takes 3-6 months for eggs to develop and mature. As the eggs are developing, they transition from a primordial, to preantral, and then to an antral follicle. Antral follicles are visible by vaginal ultrasound. [Leon Speroff and Marc A. Fritz, *Clinical Gynecologic Endocrinology and Infertility*, (7th ed.; Philadelphia: Lippincott Williams & Wilkins, 2005), pp. 104-05.]
 - 20 "Initially introduced by Rall and Fahy for mouse embryos, vitrification involves the use of highly concentrated cryoprotectant solution combined with a high cooling rate (nearly 1500 C/min) in order to achieve a glassy, solid state without causing ice formation. First applied to human oocyte cryopreservation by Trounson, vitrification is easier, less expensive and does not require a programmable freezer that is mandatory for the conventional slow-cooling method" [Emre Seli & Jacob Tangir, "Fertility preservation options for female patients with malignancies," 17 *Current Opinion in Obstetrics and Gynecology* (2005): 303].
 - 21 Other OTT techniques that need to be standardized and optimized include the freeze-thaw method, metabolic injury, ischemic-reperfusion injury (after transplantation), the optimal graft site, and the quality of oocytes matured in a graft. A September 2004 practice bulletin from the American Society for Reproductive Medicine concluded that "the cryopreservation of both eggs and ovarian tissue for cancer patients holds great promise, but at this time should remain an investigational procedure with strict oversight and be provided at no charge to patients. The report further concluded that neither oocyte nor ovarian tissue preservation should be offered or marketed as a means to defer reproductive aging." HealthLink, "Cryopreservation of Oocytes or Ovarian Tissue," 2 [available at: http://www.healthlink.com/provider/medpolicy/policies/MED/cryopresrvation_oocytes.html] last accessed 8/4/2009].
 - 22 Demesteere, "Orthotopic and heterotopic," 10.
 - 23 For example, the pea-size lumps of mature eggs in ovarian tissue that is transferred to the arm are easy to see and relatively easy to aspirate for use in an IVF-assisted pregnancy [Ibid].

- 24 Seli & Tangir, "Fertility preservation options," 304. The choice of a heterotopic ovarian graft necessarily limits the patient to an IVF pregnancy because eggs brought to maturity outside the ovarian site are unable to participate in the natural series of events of an *in vivo* conception: viz., the transport of the oocyte by the fallopian tubes to the fertilization site (the ampulla of the tube) where it is fertilized by a spermatoocyte released during sexual intercourse.
- 25 M. Rosenthal et al., "Biochemical pregnancy after fertilization of an oocyte aspirated from a heterotopic autotransplant of cryopreserved ovarian tissue: case report," 21 *Human Reproduction* (2006):2006-2009.
- 26 In a case similar to #3 of this analysis in which a woman gave birth to a full-term, healthy baby girl following a natural conception, Demeestere et al. performed two heterotopic and orthotopic transplants "to recover a normal hormonal status and to increase, as much as possible, the chance of pregnancy" [L. Demeestere et al., "Fertility Preservation: Successful Transplantation of Cryopreserved Ovarian Tissue in a Young Patient Previously Treated for Hodgkins Disease," 12 *The Oncologist* (2007):1438-39].
- 27 Demesteere, "Orthotopic and heterotopic," 3.
- 28 Ovarian graft neovascularisation is the formation of new functional microvascular networks with red blood cell perfusion in the ovarian graft. Ischemia, or the restriction of blood flow to the graft, will ensue without the oxygen and nutrients to the ovarian tissue from newly formed microvessels. Cf. Donnez, "Ovarian tissue cryopreservation," 523, 525.
- 29 Bedaiwy et al. examined published studies on MEDLINE, EMBASE, Cochrane Systematic Reviews, CENTRAL, Web of Science and Scopus databases that gave "reproductive outcomes after OTT in humans up to June 2007" [Bedaiwy et al., "Reproductive outcome," 2709].
- 30 Ibid.
- 31 Demesteere et al., "Orthotopic and heterotopic," 3.
- 32 My teleological presentation of prudential personalism relies on class material from and lengthy discussions with Benedict Ashley, OP and then on the crystallization of those ideas in his book, co-authored with Kevin O'Rourke, OP: *Health Care Ethics: A Theological Analysis*, 4th edition (Washington, D.C.: Georgetown University Press) 1997. This philosophical analysis is confirmed and expanded in the teaching of the Roman Catholic Church which reflects on the meaning of marriage, procreation, personalized sexuality, and family (Cf. *Humanae Vitae* [1968]; *Donum Vitae* [1987]; *Dignitatis Personae* [2007]) and on a humanly fulfilling way of realizing the basic human needs of procreation and family. The basis for the Church's teaching on the meaning of human procreation and for its condemnation of IVF and contraception, for example, is the personalist truth behind the inseparability principle: the procreative and unitive dimensions of a loving act of marital sex are inextricably linked. The procreative dimension of the sex act—the capacity to create a new human being—demands, defines, and activates its unitive dimension (i.e., conceiving a child within the loving act of sex as opposed to producing a child in a sterile lab, outside the mother's body and outside an act of loving union between its parents). The unitive dimension of the marital sexual act—the interpersonal communion of husband and wife within the sex act—demands, defines, and activates its procreative meaning (i.e., the openness to life as opposed to the direct suppression of fertility through contraception or sterilization).
- 33 Ibid., 206.
- 34 Ibid., 212.
- 35 Ibid., 169.
- 36 Dror Meirou et al. reported the details of this case in: "Pregnancy after Transplantation of Cryopreserved Ovarian Tissue in a Patient with Ovarian Failure after Chemotherapy," 353 *NEJM* 3 (July 21, 2005): 318-321.
- 37 [Bedaiwy et al., "Reproductive outcome," 2716].
- 38 In their journal report, Meirou et al. do not explicitly reference or describe the histological examination of the ovarian tissue to prevent transfer of neoplastic cells via the transplanted graft. However, I presume that reference to prior IRB approval for transplantation implies that this safety issue had been appropriately handled.
- 39 Meirou et al. supply the details of their transplantation technique: "Three pairs of 5-mm transverse incisions were made in the left ovary through the tunica albuginea. With blunt

dissection, cavities were formed beneath the cortex for each of the three strips. Each piece of thawed ovarian tissue (1.5 by 0.5 cm in area and 0.1 to 0.2 cm in thickness) was gently placed in a cavity, and the incisions were closed with 4/0 Vicryl sutures. In the smaller, right ovary, tiny ovarian fragments immersed in oocyte wash buffer were injected beneath the cortex” [“Pregnancy after transplantation,” 320].

- 40 Since details of this study do not include marital status or origin of the male gametes, I will presume that the sperm used to produce the human embryo or embryos in Case #1 originated from the patient’s husband, not from a donor or from a man to whom she was not married. I will also presume, in Cases 2 & 3, that the spontaneous conceptions occurred within an act of marital intercourse. The ethical issues of the first three cases, then, do not include that of breaching the exclusivity of the couple’s marriage (with their promise to be parents only through each other) by introducing a sperm donation from someone other than the patient’s husband or by denying the right of every child to be born into a committed marriage or by using sperm from a man who is not married to the patient. However, in Case #2 (and that of any monozygotic female twin opting for a syngeneic graft), the ethics of breaching the exclusivity of marriage is evaluated because it was an obvious aspect of the case: conception resulted from donor eggs.
- 41 Sherman J. Silber et al. reported the details of this case in: “Ovarian Transplantation between Monozygotic Twins Discordant for Premature Ovarian Failure,” 353 *The New England Journal of Medicine* 1(2005):58-63.
- 42 *Ibid.*, 59-60.
- 43 J. Donnez et al. reported the details of this case in: “Livebirth after orthotopic transplantation of cryopreserved ovarian tissue,” 364 *Lancet* 2004:1405-10.
- 44 Sylvia Pagán Westphal reported the details of this account in: “Doctor Pioneers New Way to Extend Fertility: Freeze Ovary Tissue” *Wall Street Journal*, Thursday, April 26, 2007, front page (available: http://www.infertile.com/in_the_new/lay/WSJ-04-26-07.htm, last accessed: 11/3/09).
- 45 *Ibid.*, 2.
- 46 W. J. Dondor works within the Department of Health, Ethics & Society (HE&S), Maastricht University and The Netherlands and the Care and Public Health Research Institute, Maastricht University. G.M.W.R. De Wert is a member of Department of HE&S and The Netherlands Research Institute Growth & Development, Maastricht University. They adjudicate the ethics of the use of fertility preservation techniques by healthy women in “Fertility preservation for healthy women: ethical aspects,” *Human Reproduction*, Vol. 24, No. 8(2009): 1779-1785.
- 47 *Ibid.*, 1780.

BOOK REVIEWS

Pharmacogenetics, 2nd edition

Wendell W. Weber. Oxford: Oxford University Press, 2008.

ISBN 978-0-19-534151-5; 433 PAGES, CLOTH, \$79.50

Doctors prescribe drugs to patients with an expected therapeutic end in mind. However, due to the variety of human responses to different drugs, drug therapy is a medical art. In *Pharmacogenetics*, Dr. Wendell Weber provides a significant update to his first edition, which appeared in 1997.

Weber divides the book into four sections: Foundations, Fundamentals, Futures, and Synthesis. “Foundations” explains the origin of the field and its defining features. Spanning two chapters, it provides a brief history and definition of pharmacogenetics. “Fundamentals” focuses on the principles of the field. The bulk of the book, this section includes seven chapters focusing on various topics, such as human drug response, age-related and ethnic issues in pharmacology, and strategies for modeling human drug response. “Futures” proposes the prospects of pharmacogenetics by discussing drug discovery and predictive biology. This explains the genetic pathways to improve drug therapy and the possibility of personalized medicine. Finally, in the brief “Synthesis” section, Weber finishes his work with a very short overview of the field.

This book presents Weber’s vast knowledge and experience in a comprehensive and approachable manner. It includes massive amounts of information placed in tables, detailing epigenetics in human disease (165-166), the history of drug discovery (310-317), and the future goals of pharmacogenetic projects (341-344), among others. Various figures illustrate applicable genetic principles.

This book serves as an excellent introduction to the field and includes enough detail to serve as a helpful reference as well. As Weber concludes, “The physician who encounters an unusual or unexpected response in practice would be well advised to question whether the responses might have a genetic basis, whether the patient might carry a known pharmacogenetic variant that could explain the response, and whether responses of such patients to other drugs might be affected” (390). This work provides an initial step in the right direction toward better understanding of this complex and expanding field.

Reviewed by Jacob William Shatzer, MDiv, who is currently pursuing a PhD in theological ethics at Marquette University in Milwaukee, Wisconsin, USA.

Bioethics: Principles, Issues, and Cases

Lewis Vaughn. New York, NY: Oxford University Press, 2010.

ISBN 978-0-19-518282-8; 686 PAGES, PAPER, \$84.95

In his preface, Vaughn states that his ambition for this book is to do what any good bioethics textbook should do in a way that is more useful and rewarding to students and teachers. For the most part, he has accomplished his goal. He combines a good basic discussion of most of the key issues in contemporary bioethics with extensive readings from original publications that reflect the major arguments from differing perspectives. Each issue-focused chapter also includes several news-making cases for students to evaluate and discuss. All of this is built on the foundation of a brief, but fairly thorough, introduction to ethics, moral principles, and moral reasoning.

Vaughn’s foundational introduction to ethics does a good job of presenting the traditional Western rational basis for moral philosophy and the primary ethical theories. When he discusses the use of moral principles in bioethics, however, he relegates Beauchamp and Childress to a footnote and presents the

“Four Basic Principles” as autonomy, beneficence, utility, and justice rather than the more commonly accepted principles of respect for autonomy, nonmaleficence, beneficence, and justice. Although Vaughn is presenting ethics from the standpoint of secular rational philosophy, he acknowledges and discusses the place of religion in ethics. However, his discussion of Divine Command ethics suggests that he does not fully understand Christian theology, and his discussion of Natural Law confuses natural law theory itself with Roman Catholic ethics. It should be noted that, although much of Roman Catholic ethics is based on natural law reasoning, natural law theory is broader than its Roman Catholic applications. It should also be noted that Vaughn confuses the Christian concept of sanctity of life with vitalism, a distinction that needs to be elucidated for students. If this text is used in a course designed to present both a secular and Christian view of bioethics, then a better foundation in Christian ethics needs to be supplemented, and Vaughn’s misunderstandings of Christian ethics need to be clarified.

Chapters dealing with specific bioethical issues cover most contemporary issues with the exception of transplantation ethics and trans-humanism. In the section on the physician and the patient, Vaughn covers issues such as paternalism, confidentiality, and informed consent, showing an appreciation for the importance of these day-to-day issues. However, end-of-life care and the withdrawal or withholding of life-sustaining treatment (among the most common issues in clinical ethics) could be dealt with in more detail. Issues regarding embryonic stem cells would seem a better fit with the discussion of reproductive technology rather than genetics. Otherwise, the structure of the book lends itself well to structuring a one-semester college class.

For the most part, issues are presented in a balanced way, although the author’s viewpoint inevitably comes through. Classic case files, excerpts from legal cases, cases for evaluation and discussion, and readings from ethics literature add significantly to the basic text and are the features that make this textbook unique as well as worthwhile for students. Even so, the sections on applying major theories as well as the summary at the end of each chapter are less helpful. In spite of some limitations, though, Vaughn’s book has proved to be a very helpful textbook for a college level course in bioethics, and I will continue to use it for future classes.

Reviewed by Stephen A. Phillips, MD, MA (Bioethics), who has practiced Family Medicine for twenty-nine years and is currently teaching Medical Ethics and helping to develop a Center for Christian Ethics at Taylor University, Upland, Indiana, USA.

This Mortal Flesh: Incarnation and Bioethics

Brent Waters. Grand Rapids, MI: Brazos Press, 2009.

ISBN 978-1-58743-251-4; 205 PAGES, PAPER, \$21.99

Composed of a diverse collection of past talks and previously published articles, Brent Waters’ book centres around a single theme. Directing himself to Christians, particularly Christian bioethicists, Waters warns the reader about the dangers of what he identifies as a postmodern ideology, with a focus on the dangers of postmodernism insofar as it has a bearing on, or affects, the use of biotechnology and the practice of medicine.

Christian teaching and faith are pitched against postmodern attitudes and aspirations. Postmodernism is described as heretical from a Christian perspective. Thus, Waters argues that postmodernism represents a form of Gnosticism, harbouring Pelagian aspirations. It is also, he says, a Manichean form of Gnosticism because – like the ancient Manicheans – it sees mortal flesh, that is, the human body, in a negative light. Placing a high value on human intellectual capacities, independence and autonomy, Waters argues that postmodernism identifies the person in Lockean dualist terms with his or her intellectual abilities. By doing so, postmodernism denigrates the body.

Waters describes postmodernism as Pelagian because it promotes belief in human salvation by means of human rather than divine agency. But, as St Augustine of Hippo argued, to promote such belief is to foster false hopes and vain aspirations, for only God can save us. And God, our triune God, saves us not for a utopian and immortal existence in this world but for eternal union with Him in Heaven.

Waters notes that a Christian understanding of the body is as an integral part of a human being. Together with intellectual or mental faculties, the body constitutes the person an individual is. As such, the human mind, as well as the human body, is made in the image of God. Or better, it partakes in the image of God. For this reason, the body is seen as good. By contrast, Waters observes, while postmodern humans cherish the body to the extent that they adore bodily youth and health, in reality they take a dim view of the body, because it is as bodily creatures that they are frail and mortal beings.

Linking the body to human frailty and mortality, the postmodern seeks to enhance the body and, with it, the person it houses. Not content with medicine as a caring profession seeking to alleviate suffering and allowing the possibility of healing, the postmodern asks for far more from the newfound powers of medicine and biotechnology: perfection and immortality. Placing hope and faith in medical advances in areas such as genetics and stem-cell research, coupled with nanotechnology and computer technology, the postmodern wishes to conquer human fragility and death.

Weeding out the unfit before they are born and using embryonic cells to enhance and prolong adult life, the postmodern fails to recognise the risk of stagnation. While seeking perfection in their children, the postmodern humans are actually anti-natal, Water argues. This comes to the fore, of course, especially in their quest for their own immortality. If immortal, there will be little need for new births. In a quest for immortality, then, the postmodern fails to recognize the need for the new generations that bring novelty and change.

Moreover, by pursuing immortality, the postmodern will eventually blur the line between nature and artifact. In an effort to enhance human powers by tampering with human nature or by creating bionic men and women, a new kind of humanity will be created – men and women who are half artifact (or machine) and half natural mortal flesh. In a quest for immortality and perfection, postmodern humans risk creating something other than human.

Over and over again Waters warns us not to be seduced by postmodern aspirations. While the healing powers of medicine and biotechnology may be welcome, salvation is not from medicine and biotechnology. His is a powerful warning to Christians not to succumb to idolatry and the worship of false gods.

Reviewed by Agneta Sutton, PhD, Lecturer in the Department of Pastoral Theology at Heythrop College in the University of London, UK.

Persons, Humanity, and the Definition of Death

John P. Lizza. Baltimore, MD: The Johns Hopkins University Press, 2006.

ISBN 0-8018-8250-8; 212 PAGES, CLOTH, \$45.00

The definition of death within the clinical arena has undergone significant changes with the advent of modern medicine. Prior to the mid-twentieth century, when medical technology began to rapidly progress, death was recognized to have occurred at the time of cessation of spontaneous heartbeat and respiration. The development of ventilators and other life support systems has enabled medical practitioners to suspend, and in many instances prevent, the death of a patient suffering from a previously fatal injury or disease process. This does not come without a cost, however, and in many instances the cost is the loss of an easily identifiable point of death. This is exemplified in the case of the person who has suffered a significant neurological insult to the point of brain death but, with the help of machines, still has a heartbeat and respiration. Clinical medicine, in this instance, accepts the complete and permanent loss of whole brain function as the death of the patient. John P. Lizza is critical of this paradigm of death, believing that this is a reductionist view. Lizza has spent much of his academic life researching the problem of defining death using different concepts of persons and personal identity.

The text begins with an examination of how the biological paradigm of death came to be established. Lizza argues that the three biological definitions of death proposed by theorists working in the area fall short. He then discusses three concepts of personhood and how they affect the definition of death: a

species view in which the person is identified with the human organism or body, a functional view in which the person is related to abilities or certain degrees of awareness, and a substantive concept that considers the person as a substance with psychological and corporeal characteristics. He argues that the proponents of each of these views cannot agree because they are using different concepts of the person and are thus arguing about the death of different kinds of things. The view Lizza favors is a substantive one, arguing that it provides the proper conceptual perspective for a consciousness-related definition of death. His opinion is that only a nonreductionist view of persons is morally appropriate, and he believes that this is the view with the most public support.

Lizza concludes his book with a discussion of the effect that changing the biological paradigm would have on public policy. His position remains that the current practice of determining death by strictly biological criteria is reductionist, is not consistent with many philosophical views, and is not the view held by the typical layperson. He argues that a more pluralistic approach be taken when it comes to defining death, an approach advocating the loss of the psychophysical integrity of the person. His argument is that this allows for a determination of death consistent with different religious and philosophical perspectives.

John P. Lizza has written an important work in *Persons, Humanity, and the Definition of Death*, arguing for a deeper understanding of humanity and the death of the person. The work is technical in nature and largely secular in its arguments; nonetheless, it adds another piece to the puzzle.

Reviewed by Jeffrey G. Betcher, MD, FRCPC, MA (Ethics), who practices anesthesiology and critical care medicine at the Regina Qu'Appelle Health Region in Regina, Saskatchewan, CANADA.

Aquinas on the Emotions: A Religious-Ethical Inquiry

Diana Fritz Cates. Washington, DC: Georgetown University Press, 2009.

ISBN 978-1-58901-505-0; 288 PAGES, PAPER, \$29.95.

Diana Fritz Cates's work on Aquinas and the emotions provides a helpful resource for both Aquinas scholars and those who are interested in understanding the operation of human emotions. It provides a helpful understanding of a somewhat neglected area of the *Summa* while also demonstrating the relevance of Aquinas's thought for those who may disagree with him on other points, for he "leads one to ask important questions of any account that one might not otherwise think to ask, and the level of care with which he tries to answer these questions raises the bar for others." (257)

Cates's introduction provides a helpful outline of the book. In the first two chapters, she provides a little bit of background by explaining her understanding of religious ethics and the study of emotions in the field. Chapters three and four lay a foundation for later chapters by defining emotions. Chapters five and six focus on emotions as "sensory appetites," approaching the topic "from below" by relating humans to nonhuman animals. Chapters seven and eight work "from above," referencing Aquinas's scale of being, since humans are more than animals. Chapter nine provides a synthesis of the previous two, demonstrating a circularity in which emotions can influence intellectual acts, which can also affect the formation and course of emotions, etc. Finally, in chapter ten she draws together the various strands of the book and assesses its value for the field of inquiry.

Aquinas "thinks that emotions, like everything else in the universe, exhibit certain patterns and follow certain laws. Emotions (as he defines them) have a formal structure, and they exhibit a kind of logic." (248) According to Cates, there are four notable features that make Aquinas's way of thinking about the emotions significant. First, he "holds that emotions are modes of tending in relation to objects of perception or imagination that we assess to be significant for our own or another's well being." (9) This connects to two important features of how the emotions work: they tend toward perceptions, which humans have in common with animals, but they are also related to the imagination or intellect, by which humans are able to evaluate and reflect. This ties into the second notable feature: Aquinas "attends to the cognitive while also attending to the appetitive dimensions of emotion." (10) His account maintains

a complexity by not reducing emotions to pure reaction or pure intellect. Third, he “allows us to notice significant structural similarities between the object-oriented appetitive motions of humans and [those] of other, nonhuman animals.” (10) Fourth, his account has “remarkable metaphysical depth” when placed in the context of his systematic theology. (11)

Cates’ work is helpful because she shows that the emotions are best located in the midst of “dynamic, reciprocal, causal activity” between human senses, dispositions, intellectual acts, and the will. While humans cannot entirely control emotions, they can cultivate virtues that work into the dynamic equation to help respond in a way tending toward the good.

Reviewed by Jacob William Shatzer, MDiv, who is currently pursuing a PhD in theological ethics at Marquette University in Milwaukee, Wisconsin, USA.

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VOL 27:2, SUMMER 2011
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