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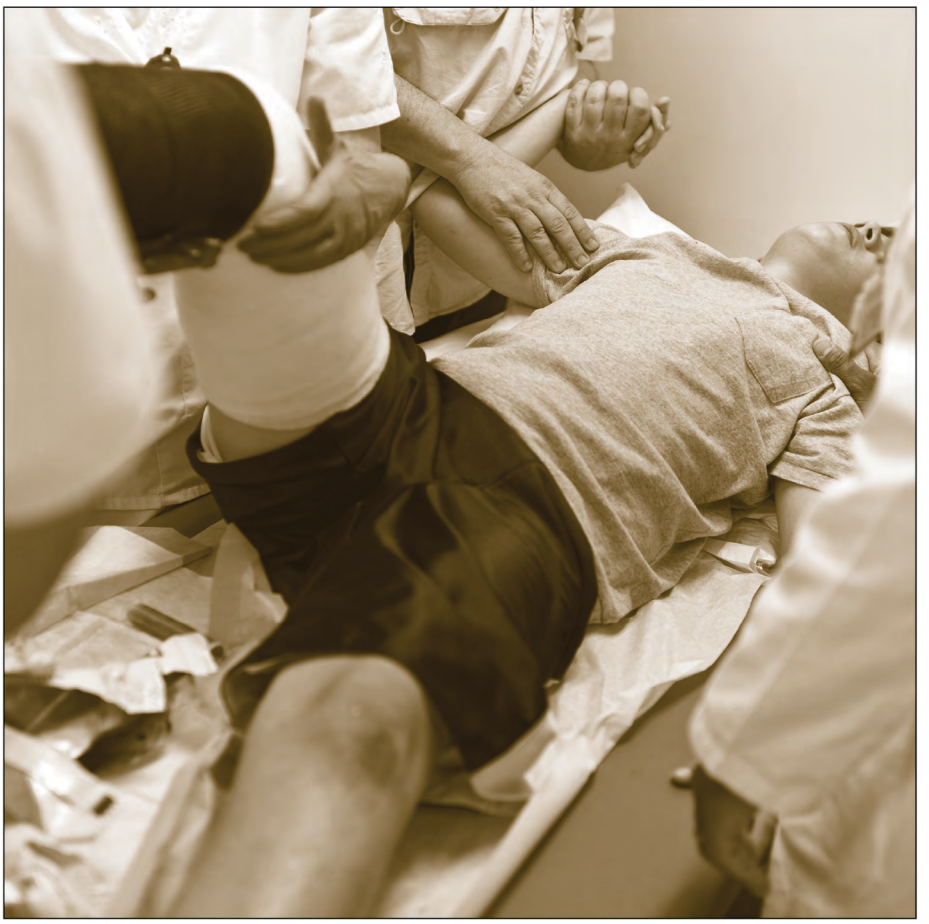

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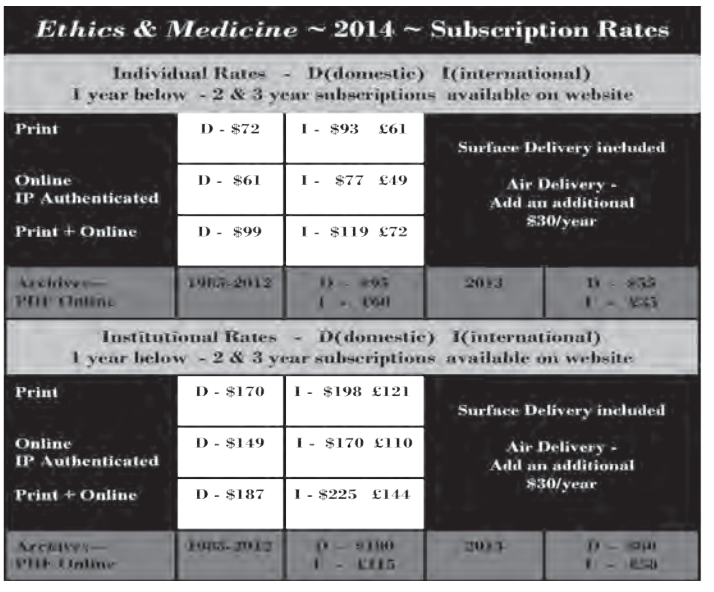

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EDITORIAL

# The Human Commodity Nightmare

C. BEN MITCHELL, PHD

In my dream I heard faint but festive music. As I neared, I could just make out the bouncing notes of the calliope wafting through the air: dat, dat, dada dada, dat, dat, dada. It was a fair! From a distance I could see hoards of people crowding the midway. Yet the sights, sounds, and even the smells of this fair were very different from those I'd experienced in the past. No cotton candy, cracker jacks, or corn dogs. Nor did I find a single carney game with its iconic giant stuffed teddy bear, which no one ever won. No, this fair was different.

I approached a kiosk that advertised the sale of human organs. The special that day was on kidneys. Surely this was a nightmare. No one would put human tissues and organs on the auction block. Yet, here they were. And even fetal body parts were on offer. Fetal tissues for sale: how macabre. The sales representative was dressed smartly. He spoke in calm and soothing tones as he handed me a price sheet, reminding me, "you never know when you might need these."

One woman gazed longingly at the merchandise. She had parked a pram holding a baby to the side, and her small daughter stood nearby. The woman, obviously pregnant, was looking at the blown glass vials in which were stored the elixir of life: stem cells of all varieties. Personal bar code stamps were available for each family member. There were entire embryos here also—no doubt surplus ones from the fertility clinics. Oh, and there was a 'Build a Boy/Build a Girl' machine! Why hadn't she thought of that earlier? A little girl with musical talents would be such a nice addition to the family! Perhaps the next time, if there was a next time. The government, it seems, had place a limit on the number of offspring in each family.

The next kiosk rested under an elaborate awning. Above was the banner: '*C'est Moi* Boutique.' Summoning my high school French, I came to understand this was a designer boutique of a very strange sort. 'It is I' was not selling cosmetics, hair care products, or imported fabrics. It was offering the ultimate in self-design. However, just as in the finest fashion boutiques, there was a small library of catalogues with jaw-dropping choices. 'DIY Genome' offered the latest in somatic cell re-engineering. " Need a few extra IQ points? Never been easier!" "Want to keep those unwanted pounds off forever? Tweak your metabolism through genetic enhancement." "Keep forgetting where left your keys? Get a memory boost through genetics!" "Not satisfied with nature's roll of the genetic dice? Let us help!" Bold promises indeed. And there, just in the corner of one of the bookshelves, I saw it, a goose. And just where you thought it would be, a golden egg. What a fitting symbol. What's next, I asked myself, a fountain of youth?

I saw a couple holding hands, peering wistfully into the boutique, wondering if these enhancements could be theirs. But, judging from the price tag on some of the services, only the very rich could access the Gucci equivalent of self-design. After all, one of the keys to the marketplace is creating a felt need that makes people reach deep in their pockets to enjoy the pleasures of the rich and famous. Manipulating one's genome makes designer handbags look like plastic bags at a big box superstore.

I watched carefully the people coming into the last booth. Their faces were amazingly beautiful. Their bodies were toned, and many tanned, but none overmuch. Their teeth were pearly white and perfectly even. No noticeable scars or wrinkles marked their faces. Even those with white hair—which were few, indeed—had no sagging chins. I walked toward a man about my own age, as he walked toward the lady at the counter. He didn't slow his pace as I approached. We were about two feet apart, and then there was no intervening space. Our bodies collided but I felt no pain. The collision, if one could call it that, lasted a second or less. He didn't stop; he didn't have to. He passed right through me, ephemeral and ghostly.

Then I asked myself, could this truly be the future of our humanity? What is the cost of turning our humanity into a commodity to be bought, manipulated, augmented, and sold? The answer seemed so clear to me in my dream. The cost of commodifying our humanity is losing our humanity.

And with that realization, I awakened in a cold sweat. **E&M**

GREY MATTERS

# Miniature Human Brains: An Ethical Analysis

WILLIAM P. CHESHIRE, JR., MD

*I began to think myself in Lilliput.* – Jonathan Swift[1]

## Abstract

*The recent creation of human cerebral organoids resembling miniature brains has opened a new chapter in neuroethics. Ethical analysis of this innovative biotechnology begins with a comparative examination of the biological constitution of brain-like entities, followed by consideration of the moral status of isolated brains, the potential benefits to medical science in the prevention and treatment of neurologic disease, and potential health risks of neural transplantation. Whereas these experiments touch on philosophically fascinating questions about what it would mean to have brains without bodies, thankfully such morally disturbing prospects remain beyond the reach of neuroscience for the foreseeable future.*

## Introduction

Regenerative medicine's most intriguing aspiration is to coax pluripotent stem cells into assembling into functional organs to replace failing organs in patients.[2] Realization of that prospect, which some have called the "Holy Grail" of medical science,[3,4] could profoundly transform the face of medicine, if not also how we think of the human body.

The tissue least amenable to engineering from cell culture to fully functioning organ may be neural tissue, as the brain is by far the most intricate and complex of human organs,[5] which is why a paper recently published in *Nature* is noteworthy. Madeline Lancaster, who is the Marie Curie postdoctoral fellow in the laboratory of Juergen Knoblich in Vienna, in collaboration with colleagues in Austria and the U.K., has successfully induced human pluripotent stem cells to aggregate into self-organizing three-dimensional tissues resembling miniature brains.[6] The neural aggregates grew to pea-sized (4 mm diameter) globules and, bathed in a nutrient mixture, could be maintained for several months in a spinning bioreactor.

## What They Are

When examined under the microscope, the cellular architecture of the Viennese entities was found to recapitulate the developing human brain. Continuous neuroepithelia surrounding a fluid-filled cavity formed complex, heterogeneous, rudimentary brain structures morphologically reminiscent of the cerebral cortex, choroid plexus, and retina.[6] So novel are these brain-like neural aggregates that the researchers invented a new term – cerebral organoids – to describe them accurately.

Cultured cerebral organoids afford a useful *in vitro* model in which to study the early development of the human brain under controlled laboratory conditions. They could be used to study human species-specific aspects of embryological neurodevelopment that are unavailable in mouse or other animal models. Studies of cerebral organoid growth might, for example, identify the particular profiles of gene expression and epigenetic influences that direct the initial stages of neuronal migration in their mysterious trajectory toward forming the mature human brain.

Cerebral organoids could also be used as reductionistic models to study disease-specific neurodevelopmental disorders, such as autism spectrum disorder, epilepsy, trisomy 21, fragile X syndrome, familial dysautonomia, and nutritional and toxic causes of neurodevelopmental delay. Until now much of our current understanding about developmental neurobiology has relied on postmortem brain tissues. The knowledge gained from studying more accessible sources of organized brain tissue might lead to new ways to prevent and treat these devastating disorders.

Cerebral organoids could even be used to study patient-specific neurodevelopmental disorders, advancing neuroscience a step closer to individualized medicine.[7] Lancaster and colleagues demonstrated this by growing cerebral organoids from stem cells derived from an individual patient with a genetic form of microcephaly. In the patient-derived organoids they found that the neural tissues were smaller with premature neuronal differentiation.[6] Their findings surpassed what it had been possible to learn through animal models.

Further practical value of cerebral organoids may lie in their potential usefulness as an organic substrate on which to conduct tests of the pharmacologic effects and toxicities of new drugs that interact with neural tissue. Several decades ago, the development of cultured human cell lines represented a seminal advance in biotechnology that led, for example, to the development of vaccines for polio. Cerebral organoids represent a further refinement in tissue culture biotechnology that promises to bring within reach the ability to evaluate early neurodevelopment in the context of specific diseases or under the influence of neurotropic drugs.[8]

Currently, the cost of bringing a new drug to market in the United States is estimated at between $1.3 and $1.8 billion.[9-11] Some of this cost comes from preliminary drug studies to assess biologic effects and toxicity on neural tissue. If data that is currently obtainable only through animal models could be furnished by conducting studies on cerebral organoids, which would be a paradigm shift in drug development, then it might become possible to lower the cost of testing new drugs and also to decrease the time needed to conduct the research required to gain approval by the Food and Drug Administration. Human cerebral tissue may also have biological advantages over nonhuman animal tissue, since currently 92 out of every 100 drugs that successfully pass animal trials subsequently fail human trials.[12]

In these ways cerebral organoid biotechnology may have the potential to enlarge the repertoire of available neurological drugs and vaccines, decrease the cost to society of new drug development, and bring new drug discoveries to the bedside sooner.

## What They Are Not

In his book *That Hideous Strength*, C. S. Lewis describes the intuitive revulsion one might feel when confronting a living, thinking, human brain, severed from its body and kept alive unnaturally through technological means:

> I thought I saw a face floating in front of me… there didn't seem to be anything above the eyes. Not at first. But as I got used to the light, I got a horrible shock. I thought the face was a mask tied on to a balloon thing. But it wasn't, exactly… What it really was, was a head (the rest of a head) which had had the top part of the skull taken off and then… then… as if something inside had boiled over. A great big mass which bulged out from inside what was left of the skull… You could see it twitch. Even in my fright I remember thinking, "Oh kill it, kill it. Put it out of its pain."[13]

Contrary to sensationalist media depictions of "test tube brains,"[14-16] cerebral organoids are not actual brains. In an accompanying editorial, Oliver Brüstle points out that "the realization of a 'brain in a dish' remains out of reach," because the organoids lack the full spatial organization of the human brain as well as a circulatory system to allow further growth and development.[17]

At only 4 mm in diameter, their volume is one thousandth that of a mouse brain and one millionth that of an adult human brain. There is, of course, no formula for converting the number of neurons present to the depth and quality of thoughts that a sufficient number of neurons in their natural milieu might generate. No one knows how many neurons it would take for a distinctively human thought to emerge.[18] Notwithstanding this uncertainty and the empirical problem of even detecting such a thought, it is interesting to note that a cerebral organoid is approximately ten times the size of the brain of a honey bee.[19] Honey bee cognition, while limited, is not trivial; it comprises the capacity to interpret visual and social cues, navigate its home geography, assess distance and direction. Bees can also evaluate the plausibility of potential food sources, which biologists regard as a rudimentary form of imagination.[20] The honey bee brain, however, is designed for honey bee activities, such as buzzing around a hive, whereas a human cerebral organoid that aggregates transiently within a spinning bioreactor has no innate purposeful composition relevant to its environment and no bodily correlate.

In an age of ever intensifying microelectronic computational power that, in some respects, rivals human intelligence, cognitive criteria alone, though important, seem to be increasingly inadequate for defining human beings or understanding what about them is unique. Essential also are the meaning of embodiment and ontological status as a member of the human species.

A normal human brain develops, not in isolation, but within and as part of an integrated body. A body is not an inert structural container for the thinking brain, but rather is a sensitive interface through which the brain perceives and interacts with its environment. The body is also a conduit for intentional movement and creative expression. Hypothetically, if it were possible for a brain to be grown to a mature size in isolation, without a body, such a brain would not be, nor could it become, a person. Persons as embodied beings inhabit the world in a likeness that is shared by others while also being individually unique.

Cerebral organoids are not detached brains, since at no time in their development are they ever joined to bodies to relay sensory information from the environment, which

may be a necessary precondition for a brain capable of thinking thoughts that correspond to external reality. Absent a body or any peripheral sensory information from vision, hearing, or touch, a cerebral organoid would have no means of developing an awareness of its surroundings or even its own existence, let alone that of others.

In regard to ontological status, the embryoid bodies that formed cerebral organoids in the report by Lancaster and colleagues from the beginning lacked the capacity to develop into a human fetus, child, or adult. The induced human pluripotent stem (iPS) cells from which they were grown, which were derived from skin fibroblasts, also lacked such capacity. However, the researchers conducted parallel experiments using human embryonic stem cells (H9, WiCell), which were originally derived from human embryos at the Technion-Israel Institute for Technology. For those who consider it morally wrong intentionally to destroy nascent human life for the purpose of embryonic stem cell procurement,[21,22] the use of stem cells lines derived from those embryos raises difficult questions of moral complicity with the prior taking of innocent human life.[23]

These ethical concerns are alleviated by the researchers' finding that "cerebral organoids could be reproducibly generated with similar overall morphology and complexity from both human embryonic stem (ES) cells and iPS cells."[6] Therefore, this research supports the conclusion that it is not necessary to destroy human embryonic life to obtain useful cerebral organoids.

## What They Might Become

Looking ahead to further potential applications of cerebral organoid biotechnology, the prospect of transplantation may eventually arrive. Whereas whole human brain transplantation would be neither feasible nor desirable, patients with brain or spinal cord damage from stroke, trauma, encephalitis, or focal degenerative disorders might benefit greatly from transplantation of viable neural tissue, provided that the transplanted tissue could functionally integrate with, and not disrupt, the patient's own nervous system.[24]

Imagine a spinal cord graft for Christopher Reeve for his paralyzing cervical spine injury, anterior horn cell grafts for Lou Gehrig to treat his amyotrophic lateral sclerosis, substantia nigra grafts for Michael J. Fox to treat his Parkinson disease, hippocampal grafts for Rosa Parks to treat her Alzheimer disease, or a frontal lobe graft to restore moral awareness to injured railroad foreman Phineas Gage. Such grafts, if they could be engineered, would not in all likelihood achieve full restoration of neurologic function, but they might provide the best possible regenerative treatment obtainable through medical science.

A considerable amount of research is needed before such dreams of regenerative medicine could be realized. In addition to deciphering the multitude of precise cellular conditions and chemical signals needed to induce cells to differentiate into viable neurons that can survive and functionally integrate with host neurons, a number of safety concerns should be addressed. We must be certain that cells grown in a laboratory dish and implanted into a patient will not, once established in the target tissue, continue to grow and form brain tumors. We must be certain that the implanted cells do not harbor potentially lethal latent infectious agents such as endogenous retroviruses or prion diseases – which might also be a concern for vaccines developed on cultured neural tissue. Finally, we would prefer that implanted tissue match the patient's own cellular composition closely enough

to evade immune rejection, so that the patient does not have to commit to a lifetime of expensive and potentially harmful immunosuppressive drugs.

Within the safety and ethical constraints discussed so far, this writer considers the development of cerebral organoids to be ethically permissible and its potential medical applications in general to be ethically praiseworthy.

As forethought is an indispensable aspect of ethics, there are further possibilities to ponder. Stretching the imagination toward a distant possible future, depending on how it is developed, this (as any) biotechnology might also carry the potential to spawn some troublesome ethical problems.

Currently, cerebral organoids grown to 4 mm, which appears to be the upper limit for growth in the laboratory in the absence of a circulatory system, model just the earliest stages of neurodevelopment. Subsequent stages of development, including neuronal migration, axonal and dendritic outgrowth, branching, myelination and other neural-glial interactions, synaptogenesis, synaptic pruning, and connectivity, are also of scientific and medical interest, and the development of living models of these phenomena may eventually be pursued. If it were to become possible, through, for example, an artificial circulatory system, to grow more developmentally advanced cerebral organoids with greater and greater functional capacities, where, then, should the ethical line be drawn that delimits how far along the developmental pathway such entities should be created? What would count as a morally significant boundary? Would it be brain volume, number of neurons, structural complexity, computational processing, abstract thought, language, ability to respond to threat, self-awareness, or some other measurable emerging characteristic? How might the earliest indications of such capacities in tiny organoids be detected? Do immeasurable qualities also matter?

The goal of finding better and better human disease models could translate to designing living entities that resemble ever more closely human structure and function. The more useful biological brain models were to become, it may be that the more human they would seem. Whether future versions of human cerebral organoids, monitored and connected to their environment by microelectronic interfaces – interfaces that might also function as sensory prostheses, as a kind of body, would or should be recognized as members of the human community might not always remain a question solely dealt with by science fiction. As long as morally concerned people remain interested in biomedical science, there will continue to be new and interesting questions with which to grapple.

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CLINICAL ETHICS DILEMMA

# COMPROMISING THE ETHICIST

ANONYMOUS

**Editor's Note**: *This column presents a problematic case – one that poses a medical-ethical dilemma for patients, families and healthcare professionals. As the case is based on a real situation, identifying features and facts have been altered in the scenario to preserve anonymity and to conform to professional medical regulations. In this case the hospital ethicist discovers disturbing personal information.*

**Column Editor**: Ferdinand D. Yates, Jr. MD, MA (Bioethics), is Professor of Clinical Pediatrics, State University of New York at Buffalo, and Medical Director for Neighborhood Health Center in Buffalo.

## Question

How should an ethicist respond upon discovery that the salary source is from an agreement that prohibits fair competition and access to quality medical products?

## Case Study

A middle-aged ethicist was in the process of interviewing for a paid position as Medical Ethicist in a moderate-sized teaching hospital in a northeastern state.

As interviews were nearly complete, a handshake was offered, and the ethicist was told that the draft of the contract was in the lawyer's hands, and that the papers should be completed within a few weeks. The ethicists' malpractice insurance was to be provided under the hospital umbrella insurance. In the meantime, the Hospital President (also the Chief Executive Office – [CEO]) of the hospital suggested that the ethicist meet with the administrative team and subsequently provide written documentation of the purpose of and benefit for the hospital and hospitalized patients.

The ethicist developed a hospital-based teaching and consultative service, and with administrative support, was asked to consult on ethical dilemmas regarding the patient care and proposed medical treatment of hospitalized patients. Because of the official consultative process, the ethicist was also able to obtain direct payments for consultative services directly from several of the local insurance companies.

At the end of the first year of service, the contract was agreed upon and signed; as a one-year contract, it would provide for a second year of consultative services for the hospital.

Toward the end of the second year of work at the hospital, the ethicist was made aware of a particular medical supply agreement within the hospital. Apparently, the hospital administration had agreed to participate in a single-sanction formula arrangement, where every non-breastfeeding mother was discharged home with a specific formula and advertisement paraphernalia for that particular formula and supporting products only produced by the parent company. Mothers were told that this particular formula was the hospital's choice recommendation for the infant, and there was not-so-subtle coercion

on the new mothers to continue using this particular formula product. Allegedly, a substantial financial contribution had been made by the formula's parent company to a recent construction project within the hospital system.

The ethicist attempted to contact appropriate individuals within the hospital who might have been knowledgeable of the formula arrangement, but no phone calls were returned. Ultimately, the ethicist was informed that the purchasing department was in a state of flux as a senior official was no longer employed by the hospital.

Sometime later, during casual conversation between the CEO and the ethicist, the issue regarding the formula choice and financial arrangement came up for discussion. The CEO clearly seemed pleased with the financial arrangement, and unabashedly informed the ethicist that a part of those monies had been specifically set aside to fund the ethicist's salary as the hospital budget had never been changed to reflect the ethicist's position as a hospital employee.

## Discussion

It is possible to compromise an ethicist in a variety of ways.

The professional physician is well-aware of the importance of documented qualifications and discoverable practice patterns. The typical physician has been trained to expect comments and queries regarding his services (in the form of training, teaching, patient care, research and administration), his qualifications (in the form of licensure and professional documentation, and his testimony (in the form of published document, presentations, malpractice experience and professional sanctions). As these areas are open to public scrutiny, the physician-ethicist should face no challenge in this arena – assuming that there is no inappropriate activity.

In contrast, however, most physicians have not received adequate training regarding the matters of personal and corporate finance. In fact, nearly all young physicians proceed into a professional career with an altruistic goal and a substantial personal debt – both related to the professional education. As such, they are pleased to receive a reasonable salary and give little – if any – thought to the source of their new-found income. As such, a curious and untenable situation arises when the financial stream for a salary is from unfair and discriminatory hospital administrative behavior.

To no one's surprise – except the physician's – an external assault on the physician's financial package is often totally unexpected. The unjaded physician has few resources for assistance in this sort of conundrum and, oftentimes, simply must self-represent.

## Case Continuation

In this case, the ethicist was well-aware of the implications of the information provided by the CEO. News of the 'formula deal' was spreading throughout the community, and the ethicist learned more about this issue from outside the hospital system than from the hospital administration. The competing hospital system had been contacted by both formula companies for distribution access to the nursery, and the nursery administration elected to set up a 'rotational system' where the parent companies would be given equal exposure, on a rotational basis, for the privilege to provide non-breastfeeding mothers with their formula products. The ethicist personally knew both local formula representatives (having played golf with each of them on numerous occasions), and each was asking

for concessions favorable to their respective companies – the one whose formula was excluded from the ethicist's hospital legitimately claiming discrimination and that the hospital 'deal' was unfair and exclusionary. It would not have been unexpected for the ethicist's personal financial remuneration to become public knowledge as this situation and its nuances filtered through the local medical community.

Should the ethicist resign? Should the ethicist ask that the CEO redirect the source of the ethicist's salary? Should the ethicist campaign for a rotational formula program within the hospital's nursery?

## Denouement

At the end of the 2nd year, a short time after the revelation of the source of the salary, the ethicist's contract was not extended.

## Editor's Comment

Situations such as this financial funding issue provide a most effective way of potentially discrediting the professional physician. Such an assault may not only attack the professionalism, but may substantially undermine – and as in this case may effectively compromise, or ever prohibit – the work of the physician. Discrediting the ethicist may well remove the voice and the platform. A useful and appropriate message for ethical medical care in the hospital may not be heard if there is no one listening.

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## THE NEW MEDICINE: LIFE AND DEATH AFTER HIPPOCRATES
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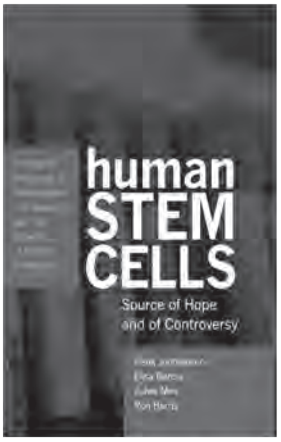


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# Ethical Issues Raised by Compassionate Access to Experimental Therapies

JAMES J. RUSTHOVEN, MD, MHSC (BIOETHICS), PHD

## Abstract

*New therapies for various diseases are being developed and approved at an increasing rate. New biomarkers are helping to predict what patients may benefit most from specific new treatments. However, there has been a tradition within the area of drug development whereby patients with advanced, often life-threatening illness may seek, and be given access to, new but as yet unproven therapies. Some advocacy groups have sought legal and legislative approval for access to experimental therapies even at very early stages of development where efficacy and sometimes safety are uncertain and, thus, risks of therapy are high. Some such groups have claimed that patients have a constitutional right to such therapies. In this paper, short and long-term ethical concerns about early access to investigational drugs are identified and their potential consequences articulated. An appeal is made for Christians to reflect on such access practices and policies in that they often reflect misconceptions about clinical investigations. Such practices may also be inspired by a hopelessness and fear of death devoid of a biblical notion of joy in life after death for those who believe in Christ.*

## Introduction

Progress in the understanding of mechanisms of disease has led to an explosion of new therapies in the past two decades. Some of these therapies work on aberrant mechanisms of normal physiology unknown to medical science a decade or two ago. Some are designed to overcome resistance that makes previously effective treatments ineffective. While some new and effective treatments still carry significant risks of side effects associated with disease improvement or cures, many newer therapies are proving to be less toxic and more effective than previous ones, due in large part to their targeted nature. That is, such therapies are now being developed that target specific points of breakdown in physiological processes; such targets may be point mutations or other genetic or epigenetic aberrations associated with the oncogenesis of cancer. At the same time, biomarkers are being developed to identify patients whose tumours have such targets, making these patients more likely to benefit from treatment. This specificity of treatment leads to fewer normal cells being affected and thus less toxicity. Nowhere is this change in therapeutics more felt than in the treatment of cancer, a term dreaded by nearly everyone. And as the average age of our population increases, more of us will be afflicted by it or be needed to assist a loved one who is.

Over the last three decades, there has been an ongoing struggle between those who support the identification of effective and safe therapies through standard regulatory processes and others who advocate for greater access to those therapies still undergoing evaluative testing. Over the last decade in particular, there has been in increasing effort to obtain drugs under investigation at the earliest phase of human testing, well in advance of the availability of information that might allow adequate judgment about the safety and

efficacy of such drugs for public use. This article will present the history of this struggle and identify ethical issues that it has raised. While the struggle involves individuals who suffer from a variety of serious, sometimes terminal, illnesses, I will focus particularly on the struggle involving cancer patients and their advocates. Christians need to be informed about these issues. Specifically, Christians need to develop appropriate forums for discussions that identify biblical norms for these ethical issues. Such discussion can help to better prepare caregivers and patients at the end of life to make wise treatment decisions, even as death becomes the inevitable outcome.

## History of Access to Experimental Therapy

One of the key stakeholders in this struggle is the regulatory community, within which the Food and Drug Administration (FDA) in the United States has been a dominant participant. Until the 1930s, drug development in the US was regulated by a 1906 drug law. Unfortunately, this law lacked the enforcement power to prevent deceptive advertising, incomplete and inaccurate drug labelling, and poor scientific assessment of safety and efficacy. As has often happened in the history of biomedical ethics, it took a medical disaster to arouse the political will into legislative action. In 1937, 107 persons died after taking Elixir Sulfanilamide, the liquid base of which was poisonous to human beings. No animal testing had been done to foresee this disaster and, under considerable public pressure, Congress quickly passed the Federal Food, Drug, and Cosmetic Act of 1938. Under this act, manufacturers had to submit a new drug application to the new agency empowered to implement the act, showing its safety when administered to humans before marketing could be started. However, manufacturers were not required to demonstrate drug efficacy for intended uses. The agency exercised no control over clinical investigations for new drugs and no researchers or sponsors were required to notify the agency of their investigative plan for the drug.

By the early 1960s, concerns over questionable pricing and licensing practices led to a Senate inquiry, and a bill was introduced to amend the earlier regulatory act. However, again, the pace of reform quickened only when the sedative thalidomide was found to be a teratogen, leading to thousands of malformed infants born to women in Europe who had been exposed to the drug during pregnancy. A New Drug Application (NDA) for the drug was under review by the FDA at the time and the medical officer, aware of the European experience, had delayed approval on the grounds that adequate safety testing had not been done. The drug application was subsequently withdrawn. In light of this second tragedy, a Senate reform bill was modified and approved as the 1962 amendments to the 1938 act. This bill required NDA approval of an investigational drug before marketing could begin, including proof of efficacy. Over the next few years, the FDA developed standards for efficacy that paved the way for standards for designs of clinical trials involving new drugs in development.[1]

These regulatory milestones led to the current regulatory standards, which have grown out of two major principles. Firstly, research protocols must directly test for quantitative evidence of new drug efficacy against the efficacy of a control substance, using a previously approved active standard treatment of the day or a placebo control substance if no current standard treatment exists. Ideally, patients receiving the new drug or the control intervention would be treated in the same time frame and under similar conditions to avoid various confounding biases. However, historical controls could be

accepted in special circumstances. Secondly, more attention was given to the assignment of subjects to test groups; that is, the selection of human subjects was better controlled to ensure their suitability for participation in a study, patients were assigned to different test groups with minimal discrimination and bias, and formal efforts were instituted to balance pertinent patient characteristics between test groups.

This led to the division of drug development into phases. Phase I studies are small studies of generally less than 100 patients, designed to demonstrate the safest dose, route, and schedule of administration. They are the first studies in humans after animal studies have suggested possible human safety and potential efficacy. Phase II studies may involve several hundred patients altogether, sometimes but not always involving control groups, through which the first hints of meaningful efficacy are explored. If such hints are demonstrated, the drug undergoes phase III testing, wherein hundreds or even thousands of research subjects would be recruited into groups receiving either the experimental drug or control therapy. Entry into these groups is randomly assigned to ensure minimum likelihood of bias that may lead to falsely concluding that the drug is effective when in truth it is not.[2]

## Effects of Greater Oversight and Impact of the AIDS Epidemic

This increased oversight of drug development, though overdue and crisis-driven, was clearly welcomed. It represented ethical due-diligence on the part of government and its agency to protect the public from sponsors and investigators whose strategies and methods may not serve the best interests of their research subjects and, ultimately, the public. However, studies conducted in the early 1970s showed that this improved oversight and regulatory rigour was costly. One study, the contents of which were presented to a Senate subcommittee, documented that drug development costs had doubled and fewer new drugs were being introduced for clinical investigation as a result of this increased rigour.[3] Samuel Peltzman, the study author, identified the *drug lag* that involved a risk trade-off. He noted that the desired decrease in the risk of drug-related disasters among the public was also associated with greater risk of delays in approval and in public benefit of potentially effective drugs.

While the 1962 Amendments let to improved standards for clinical trial design and implementation, the use of investigational drugs outside of clinical trials actually became more acceptable and formalized. Before 1962, the FDA formally prohibited use of investigational drugs outside of participation in clinical studies. However, informal, unwritten exceptions were sometimes made. For example, drugs under development for rare disorders involved small numbers of afflicted patients, making collection of adequate data in clinical studies difficult and foreseeing that future sales may not recoup investment costs for the sponsor. Under the US Orphan Drug Act of 1983, incentives to develop and market such drugs included tax breaks and a monopoly on drug sales for seven years. When sponsors developed drugs for these rare disorders, the FDA allowed use of such drugs for patients outside of clinical trials during the ongoing investigational program.

After 1962, additional informal and unwritten mechanisms were created. One such mechanism was a “compassionate” or single patient treatment IND. This was a request by a practicing physician to obtain the investigational drug to *treat* a particular patient with a serious disorder for which the drug was being tested. Basic criteria included patient consent, willingness of the sponsor to provide the drug, and the physician will to

prescribe. However, no formal research protocol was required. The FDA tried to partly justify this action by claiming that there remained an informal research component; that is, adverse effects had to be reported to the FDA. Later, the FDA allowed sponsors to formally designate a treatment group of a clinical trial for patients to receive the drug in question without the same rigorous tracking of efficacy outcomes as the other patients on the study. While collection of safety data was fairly rigorous, this practice attempted to legitimize compassionate use by nesting it in a formal clinical trial.

Such lowering of standards of clinical trial design and testing added to the increasing confusion over what was experimental and non-experimental therapy. Patients and physicians began confusing the testing of unproven drugs with their use as treatment, as though they had been already proven effective. Such *therapeutic misconception* led to increasing demands for access to investigational drugs as advocacy groups and political representatives agitated for compassionate release of such as-yet-unproven drugs for desperate patients with serious illnesses. One prominent bioethicist later concluded that allowing new drugs that are still under investigation to become available using this parallel system for compassionate use requires that sponsors, institutional review boards, and clinical investigators must pretend to patients that such availability constitutes research when it does not.[4] As patient advocacy movements increased in number, the FDA began to formally codify its compassionate IND regulations. But then came the AIDS epidemic.

As the epidemic progressed, the FDA was under increasing pressure to deregulate the drug development process and approve new drugs under investigation earlier than the established standards warranted. AIDS activists were young, aggressive, media savvy, active in civil disobedience, and highly critical of the formal drug approval process.[5] Many argued that the FDA required too much efficacy data even for pre-approval compassionate release, that clinical trials were too scientific, and that such trials did not adequately take into account patient needs. Further, advocates argued that AIDS patients had a right to have investigational drugs for their urgent and specific medical needs. The FDA tried to formalize criteria for obtaining such drugs. These criteria included having no satisfactory alternative therapy available, including the drug in an ongoing investigational program, and requiring the sponsor to make diligent efforts to pursue formal approval. In response to activist demands, the agency formalized the parallel track drug development system, allowing for studies without controls that were conducted in parallel with controlled trials. This mechanism for securing investigational AIDS drugs could begin at the beginning of phase II testing. Eligibility for such uncontrolled parallel studies included ineligibility to participate in a controlled study and clinically significant HIV-related illness.

At the same time, the FDA devised an expedited but conditional approval mechanism for investigational drugs whereby investigational drugs could be approved on the basis of surrogate outcomes. Normally, “hard” outcomes such as cure or survival improvement are the gold standard for drug approval. Putative surrogate outcomes for improved survival might be disease shrinkage or functional improvement of the patient. However, approval using such outcomes is conditional on the conducting of post-approval (also called post-marketing) studies to show that the survival outcomes do in fact also improve. For the sponsor and patients who might benefit, such conditional approval allows fewer study patients, earlier completion of studies, and earlier release and marketing of the drug. However, this conditional approval risks that survival improvement may not be found in post-approval studies and, consequently, the drug may be pulled from the market. History

has shown that keeping sponsors compliant with completing such post-approval studies is difficult, since they have little incentive to do so in a timely fashion once physicians are using the drug and profits are coming in.

## Continuing FDA Concerns Over the Impact of Compassionate Access

The implications of compassionate access on the drug development process continued to play out in medicine in general and in cancer therapy particularly. Throughout the 1990s, debate over the appropriateness of using experimental drugs for treatment and the impact on the formal drug development system began to crescendo. Sponsors produced compassionate release protocols or support single patient IND applications from physicians for drugs under development. Some critics questioned company motives, arguing that such protocols use patients to their instrumental ends. Such ends include a desire to be perceived as compassionate by the public and to give physicians experience with their drug so that more will prescribe it immediately after approval, resulting in greater profits more quickly. Others claimed that patients in such vulnerable positions cannot make appropriate decisions regarding the true risks and benefits of such drugs. Still others noted that in participating in such protocols, any subjective impression of benefit, even from a placebo effect, could put pressure on physicians to use the drug and to make it more freely available outside of clinical studies. The physician then becomes torn between an obligation to her patient and to the public good.

Compassionate access was also discussed outside of the US.[6] In Canada, for example, a parliamentary subcommittee report recommended development of compassionate access guidelines in the mid-1990s, focusing on AIDS drugs. However, legal review criticized the report for seriously flawed arguments and conclusions. The two most important flaws were (1) the suggestion that conducting a clinical trial of an investigational drug is unethical if it is not made available outside of trial participation and (2) the claim that all patients with catastrophic illness have the right to choose any therapy as long as in doing so no harm is done to others. However, this was inconsistent with the admission that such a right does not exist in Canadian law. The legal reviewer argued that investigational therapy should only be considered when it has demonstrated an acceptable balance between efficacy and toxicity.[7]

By the year 2000, the FDA had become increasingly concerned with the implications of compassionate access for the drug development system that it oversees. This concern was particularly evident in the approval process for oncology drugs as the number of new drug submissions increased. One way the agency tried to address their concerns was through consultation with clinical experts, bioethicists, pharmaceutical representatives, and representatives of the public. This took the form of two special meetings of their Oncology Drug Advisory Committee (ODAC), one held in December 2000 and the other in June of the following year. In both meetings, participants were asked to discuss access for single patient INDs, including the ethical issues that they generate and their impact on the drug approval process.

At the first meeting, the FDA listed several issues that they often encountered in adjudicating compassionate use requests.[8] The agency acknowledged that both the public and individual patients benefit when they support and participate in clinical trials. Some patients, however, are unable or unwilling to participate. Do they have the *right* to access investigational drugs? Issues included *local or personal autonomy* wherein patients,

physicians, or institutional review boards perceive that they have the right to decide if a patient should be given access to an investigational drug. The agency noted that patients may wish to seek access, even when proven effective therapy is available, if news media or websites make claims of greater efficacy of the investigational drug that may not be sufficiently supported by research or claims that are outright misleading. Concerns were raised regarding the potential adverse effect of compassionate access on clinical trial accrual and consequently the potential to delay approval. Unbiased and meaningful data outside of a clinical trial is difficult to gather, particularly information on efficacy.

One of the bioethicists, Jeremy Sugarman from Duke University, described the changes in regulatory climates as a pendulum swing between two interpretations of the principle of justice. On the one hand, the FDA was improving its protection of the public against fraudulent treatments, and the Belmont Commission had identified three principles (respect for persons, beneficence, and justice) to guide the ethical treatment of human subjects in clinical studies.[9] On the other hand, there were now increasing demands for access to investigational drugs by individuals who claimed rights to forego participation in clinical studies and regulatory protections and to take personal responsibility for risks. He also pointed to the tendency to overestimate the likelihood of benefit by patients and investigators from phase I investigations, and the consequent misconception that the drug is therapeutic, rather than under experimental study to test for evidence of efficacy by scientific means.

Sugarman prescribed better communication of the lack of benefit of drugs in early development that allows patients to have a more truly informed and realistic understanding of potential benefits before consenting to being a human experimental subject. He particularly emphasized the need to communicate the concept of clinical equipoise. In claiming to be in a state of clinical equipoise, the investigator must be truly uncertain about the efficacy of a new drug and, therefore, should convey that uncertainty to the patient and potential research subject in order to ensure truly informed consent regarding the nature of the study. He summarized the situation as follows: "… considering access to investigational agents borders on practices of medicine and clinical research, raising some unique ethical issues." Unfortunately, while Sugarman laid out the ethical framework and language of discourse, he gave no personal ethical view as to the moral appropriateness of compassionate access.

Edmund Pellegrino also gave testimony, pointing out that the principle of autonomy had become absolutized in medicine and in the controversy over access to investigational drugs as well.[10] Limits, he argued, must be put on personal autonomy if it impacts others. For example, patient autonomy can infringe on caregiver autonomy when the patient asks for a treatment that the clinician feels is not safe or effective and thus not in the patient's best interest. While the principle of autonomy began as a negative right to allow patients to refuse treatment and avoid harm, it has expanded into a positive right to demand treatment. Pellegrino also cited studies suggesting that demands for autonomous choice actually may conceal pleas for sufficient information to make an informed decision.

Representatives from the pharmaceutical industry cited problems with diverting resources from clinical studies to compassionate access protocols and media-incited premature expectations of benefit of investigational drugs. Some promoted expanded access protocols involving multiple patients over single patient INDs as a better way to capture useful information toward drug approval. However, they failed to point out that

such protocols are not scientifically rigorous and, thus, are still rife with biases, making them unlikely to be helpful in determining the true efficacy of the drug.

The second special ODAC meeting was held six months later.[11] One private medical oncologist presented the view that the conflict between patient and physician autonomy had already been settled in the US in favour of the patient. He used this to justify making expanded access programs standard components of drug development. However, he also argued for the removal of the term "compassionate use" and for better discussion about the benefits of palliative care over anti-cancer drug therapy in terminally ill patients. Another clinician advocated for better methodology to systematically analyse efficacy information from expanded access protocols.[12] The representative of the National Breast Cancer Coalition concluded that (1) the single patient IND program was a failure, (2) the program would never be equitable, fair, or compassionate, and (3) greater effort should be exerted toward devising a better clinical trials system for more expeditious identification and approval of effective therapies. Finally, as a minority view, an investigator from the University of Michigan concluded that expanded access co-opts clinical trials by perpetuating the fallacy that there is some therapeutic benefit before it has been proven true. It also provides no valid information for determining drug efficacy. Rather, he advocated for better access to and information about clinical trials. He went so far to call it unethical, and not within patient rights, to grant patient demands for access to investigational drugs outside of clinical trials.

There were other issues raised and discussed but consensus was elusive on most of them. Most participants, however, agreed that patients should not be granted access to drugs in phase I testing where safety is being assessed and not yet determined. As the discussions wrapped up, one participant sensed that the uncertainty around phase II and even phase III trials might be sufficient grounds to not permit access outside of clinical trials. Another made the insightful comment that perhaps the FDA should formally collect information as to the reasons why patients want access to such drugs in the first place.

Two years later, in September 2002, the problem moved to forefront with the submission of the new targeted agent Iressa for the treatment of patients with advanced non-small cell lung cancer. After phase III trials failed to show efficacy for such patients not previously treated, the sponsor now sought regulatory approval for patients who had one or more prior treatment regimen. In this setting, expectations of meaningful benefit are low. Efficacy data on only about 400 patients with disease refractory to previous therapy was submitted. No control groups were included. Only 10% of patients showed evidence of meaningful tumour shrinkage, an unproven surrogate for improved survival. By contrast, approximately 18,000 patients had received Iressa off-study on a compassionate basis by time of submission, raising FDA concerns that such extensive off-study treatment gave an impression of pre-marketing promotion rather than compassionate availability. In a workshop held around the same time, an oncology medical reviewer for the FDA stated that expanded access programs could raise false hopes and that sometimes the compassionate approach would be to deny access.[13]

While the ODAC approved the drug on that basis, the FDA stalled its approval of this positive recommendation, delaying a decision until the following February and then again until May of 2003. Accused by the *Wall Street Journal* of dithering on the decision to approve the ODAC recommendation (while over 20,000 patients had now received the drug on a compassionate basis), the FDA finally granted approval, an unusually lengthy

eight months after the ODAC meeting. Part of the reason for hesitancy on the part of the FDA was the concern that physicians would start using Iressa off-label; that is, use it as front-line therapy for patients who had not yet received any treatment rather than for patients who received prior therapy. While such treatment is legal in the US, it would be ethically concerning since phase III trials testing Iressa in such patients showed no meaningful efficacy.

## Legal and Legislative Attempts to Gain Early Access to Investigational Drugs

While the regulatory community remained concerned about the role of compassionate access in drug development, legal challenges and legislative initiatives by advocacy groups were underway. In 2003, the Access Act was introduced to amend the Federal Food, Drug, and Cosmetic Act. It proposed a three-tiered approval system of drugs, biological products, and devices that would make such interventions available to seriously ill patients before regulatory approval. The first tier would involve drugs for which phase I safety data and some preliminary evidence of efficacy was available. The bill died in committee when the Congressional session ended. It was reintroduced but died in committee three more times, first in 2005 as bill S. 1956 (109th): ACCESS Act,[14] then in 2008 as bill S. 3046 (110th) in May 2008,[15] and most recently in 2010 as the Compassionate Access Act of 2010.[16] Efforts by patients and advocacy groups will likely continue through sympathetic members of Congress in an effort to get legislative sanction for a right to access drugs at the earliest stages of human testing, even when evidence of efficacy are slim or non-existent.

One high-profile advocacy group that supported these initiatives is the Abigail Alliance, named after a 19-year-old woman who died of a head and neck cancer that could not be cured or controlled with conventional therapies. She was ineligible for clinical trials of two new but unapproved drugs and died in 2001 shortly after enrolling in a trial of a third new drug. Her father established the advocacy group in an effort to lobby for earlier access to such drugs. The group blamed what they considered to be undue FDA restrictions on drug marketing during drug development, which they contended led to inadequate supply. The group initially petitioned the FDA in 2003 to broaden the criteria for accessibility of such drugs. Before the FDA responded, the alliance filed a lawsuit against FDA for failure to allow adequate access to such drugs for needy patients on the grounds that it violated a patient's right to privacy and due process.

In late 2004, the district court judge presiding over the lawsuit ruled that patients did not have a fundamental right to access unapproved drugs outside of clinical studies. However, on appeal, the appellate court judges ruled 2-1 that competent terminally ill patients with no therapeutic alternatives had the *constitutional right* to obtain potentially life-saving therapy that had passed phase I testing alone. One major reason given for the ruling cited a previous case ruling that patients had the negative right under the US constitution to reject life-sustaining treatment. From this, they reasoned an individual must also have the positive right to decide whether or not take an experimental treatment and assume the risks if there was any perceived chance of prolonging life. The dissenting judge criticized the other two judges for misunderstanding the drug approval process, arguing (correctly, in my view) that reasonable inference of drug efficacy at sufficiently minimal risk could not be established after phase I testing alone.[17] However, at the request

of the FDA, the full Court of Appeals heard the case and, in August 2007, ruled 8-2 that terminally ill patients do not have a constitutional right to access investigational drugs even when they have been established as safe after phase I testing. In 2008, the Supreme Court refused to hear the case, allowing the full Court of Appeals decision to stand, and exhausting mechanisms to gain access during the earliest phase of human testing.[18]

## Analysis of the Ethical Issues

The ethical issues of this controversy are both short-term and long-term. After the initial appellate court decision, Jacobson and Parmet wrote: "… this case raises challenging issues regarding drug safety at the limits of scientific knowledge, the role of markets versus regulators, medical care of terminally ill patients, individual rights versus protection of public health, and the allocation of scarce resources. The panel opinions offer dramatically divergent views of how to balance individual patient needs with broader public health considerations."[19] In a culture where individual rights often override the public interest, efforts to fulfill desperate hopes of extending life is understandable, even if the likelihood is small, and particularly if individuals take full responsibility for the consequences and no one else will be harmed. However, is it ethical and responsible for an individual to request treatment with a drug whose probability of helping even for a short time is very low while the possibility of an adverse event is relatively high? The following ethical concerns should be considered before the use of investigational drugs outside of clinical trials is considered.

1. *Do patients with a disease progressing toward death have a right to acquire and be treated with investigational drugs?* The legal challenge in the US suggests that they do not, at least according to judicial interpretation. But is this also true morally? Are there valid grounds to support a moral right for individuals in this situation to receive such drugs and assume full responsibility for the outcome? The moral views will depend on the worldviews that they represent. Those who believe in the merits of individualism and the right of the individual to make choices independent of other authority would likely take a "rights position." This position may also be influenced by one's belief in the meaning of death. How much time and energy should be taken to try every treatment that may have any remote or theoretical chance of benefit? Should more time be used to prepare more intentionally for death, sharing more time with loved ones?

2. *Drugs in early phase of development may not only lack efficacy but may be more risky than available data would show.* It has been estimated that only 5% of cancer drugs that begin human testing are eventually approved for human use. Among drugs that reach phase II testing due to reasonable hints of efficacy, only 30% of such drugs have sufficient promise to enter phase III testing. One study showed that 21% of investigational drugs never reach completion of clinical testing because of safety problems, 35% are terminated because of lack of efficacy, and 32% are dropped because they are deemed not economically viable.[20] These figures suggest that safety concerns at the end of phase I may still be underestimated. In addition, not all safety data is made public in order to protect proprietary interests. For example, safety results from uncompleted studies may not be submitted with the new drug applications. Furthermore, safety concerns may arise even after approval, particularly if the drug receives accelerated approval on the basis of

phase II data where the number of patients is small. Early release of drugs may therefore be more risky than is made evident from publically available data.

3. *Clinical trials may take much longer to complete if patients who are eligible to participate are also given the option to have the investigational drug outside of a study context*. As mentioned earlier, Peltzman had previously documented the slowing of drug development due to increased costs incurred by new, more stringent regulations.[21] This drug lag, as he called it, may now be further extended. That is, studies have documented that making investigational cancer therapies available outside of clinical studies correlates with a lower patient accrual rate and, consequently, longer time to complete patient accrual and to complete these studies.[22] This increase in drug lag could be due to several factors. One is the problem of therapeutic misconception. One study showed that among oncology specialists surveyed, many participants believed that the main societal purpose of clinical trials was benefit due to study participation rather than helping to gain knowledge to develop better future therapies for others. This view has been called the most important threat to the validity of informed consent in human medical research.[23]

George Annas has argued that this problem, which he calls *therapeutic illusion*, plagues the courts, Congress, and the FDA. Using a drug on study subjects is repeatedly confused with treatment given in the best interest of patients.[24] Clinical trials of new drugs are experiments, defined by testing the effects of a drug of as yet unknown efficacy and of only partially known safety. Annas rightly concludes that patients should have the fundamental right to choose their treatment, that but choices should be limited to medical alternatives that have the evidence to provide true informed consent about expectations of efficacy and risk.

Another factor that may be linked to the increase in drug lag is the inherent tension between a clinical investigator trying to fulfill a role as patient advocate as well as researcher. For the investigator, the latter role should ethically be carried out in a spirit of clinical equipoise, where the investigator is uncertain whether the new drug or intervention is better than the previous standard treatment. If honestly convinced of this, the investigator must then pass this uncertainty on to the patient who is being considered for the clinical study. If both physician-investigator and patient are convinced of this, then true research and experimentation is ethically appropriate. The investigator gains knowledge on which to build evidence for the efficacy of new treatment. For the patient, they can derive the satisfaction of contributing to the public good through contributing useful information regarding new drugs of as yet unproven worth. Depending on the phase at which the patient participates in clinical studies, some benefit may also be derived.

If, however, the investigator feels that the new drug is better by virtue of personal experience or incomplete data already collected, then this equipoise is broken and therapeutic misconception is more likely to result. In such a case, the investigator is ethically remiss in accruing patients into such a trial that is asking a question that she or he feels has already been answered (i.e., the new drug really is better therapy). The investigator should also then tell the patient that the drug could also be accessed outside of clinical trials if such is the case. When the trial in question is a randomized trial, in which there is a good chance that the patient may be assigned to the control intervention, this becomes a particularly difficult dilemma. In the development of Iressa, the much larger

number of patients receiving the drug outside of clinical trials strongly suggests that this was a problem during the phase III, randomized trials that proved Iressa to be ineffective in patients receiving chemotherapy for the first time. The low accrual to the later phase II trials involving previously treated patients, the basis of later approval, also supports this. However, unless the safety data on patients receiving the drug by way of off-study access included patients like those in the phase II studies, such a small database also ran the risk of failing to detect relatively rare but serious toxicity at the time of accelerated approval.

4. C*linical trials of a particular drug take longer to complete if off-study use for patients with advanced, incurable disease is extensive during drug development. If such a drug is approved as safe and likely to extend survival or offer cure, such delays in drug development could deprive future patients of such meaningful benefit from the drug.* Drugs that are shown to be safe and effective may significantly extend survival or cure patients in the future. In oncology, most patients who are eligible for even later phase trials of new drugs usually have advanced cancer such that they eventually die from their disease. Previously treated patients with advanced disease are usually enrolled into phase I while less heavily treated or untreated patient may be eligible for phase II or III trials. The large majority of patients with advanced cancer, except for some with relatively rare tumours such as lymphomas, are not curable, although life may be extended by months or, occasionally, a few years. However, if a drug gives some life extension and is approved, it is then often further tested through university medical centers or national clinical trials groups in patients whose visible tumour was completely resected but whose tumour had characteristics suggesting a high risk of later recurrence. For those patients, the drug in question could be curative by killing residual cancer cells that had escaped the surgery. Using such adjuvant treatment after surgery can cure many patients whose tumour would otherwise relapse and render many of them incurable. Consequently, if initial drug development has been slowed by extensive use of off-study drug, the delay may prevent many of these future patients from receiving the drug when they need it to prevent converting a curable situation to an incurable one.

5. *Granting investigational drugs outside of clinical trials erodes the FDA's regulatory authority and exerts undue pressure to approve drugs prematurely.* If the FDA continues to acquiesce to patient demands to access unapproved drugs outside of clinical trials, the power of patient rights and autonomy will likely be extended to investigational drugs for pain or disabilities. When Annas prophetically predicted that the full appellate court would reject the "rights" argument, he noted that granting such a right as constitutional would not only undermine the agency's legitimacy but would lead to a cascade of rights claims for artificial devices, controlled substances such as LSD, the right to access and self-administration without a physician's supervision, and the right to commit suicide, with or without the help of a physician or other caregiver.[25]

6. *How would a patient and physician choose the "best" investigational drug if the patient was eligible to receive one of multiple drugs being tested at some facilities?* Choosing the best among several effective treatments for a particular patient involves judging which one has the best likelihood of benefit with the least risk of toxicity. If multiple drugs were available on which there was only anecdotal efficacy data and incomplete safety

data, by what evidential criteria would the physician recommend the best one for that seriously ill patient and how would the patient exert her autonomy to decide and consent if the information is not available? In such circumstances, primary reasons for choice become fear of the unknown, fear of harming the patient, and fear of appearing to lack compassion.

7. *Drug companies take some risks in allowing drug use outside of clinical studies but also are attracted by early familiarity of physician-investigators and the public with the drug and the likelihood of earlier profits if the drug is proven effective.* In his insightful analysis of the *Abigail Alliance v. Von Eschenbach* case, Annas argued that drug companies have little incentive to make a drug available outside of trials because of the risk of reduced trial recruitment and the risk of adverse reactions must be reported to the FDA. While this may be partly true, it is also true that advanced exposure to and use of such drugs can give a major boost to successful marketing later if the drug is approved, both because of physician use and because of media and public exposure. Here, the economic and competitive advantage could exceed the concerns about drug toxicity and lower accrual, particularly if the regulator is pressured to allow early, sometime premature, approval of the drug.

## A Christian's Response to this Problem

A Christian response to this societal impasse should involve a perception of what moral beliefs are behind the positions. One of the first issues involves the confidence in the formal drug development system. Should rigorous scientific methods be used to seek the greatest confidence that new drugs are truly safe and effective? Since the AIDS epidemic, advocates for earlier access to drugs have complained that the methods have been too scientifically rigorous and do not adequately factor in individual patient desires, needs, and expectations. This scientific rigour is often considered only possible at the expense of other patient needs and the antithesis of the individual patient's best interests. What is forgotten or ignored is that the methods used are those best known to reduce bias and eliminate confounding factors that may falsely show efficacy when it does not actually exist. If efficacy is shown by such methods, there is considerable confidence that the efficacy observed among study subjects will also be observed among the larger group of patients in society with characteristics similar to the study subjects in the trials. At that point, patients can make autonomous *and* informed choices about their treatment options.

However, the real issue of many patients and advocates is not lack of faith in science but an overriding desire to address their *urgent* need. Seriously ill patients may reach out in desperation for anything that they can justify in their minds as possibly helpful, without considering fully the consequences. It is this extreme vulnerability and the fear of approaching death that often drives such decisions. The oncology community is also divided on this issue. Recently, Emil Freireich and Razelle Kurzrock framed this issue as a decision between accepting palliative care that is directed at controlling symptoms rather than trying to attack cancer cells and receiving investigational drugs. "A move to palliative care requires that the individual accept a state of hopelessness. Many patients turn to unproven remedies to restore hope." Freireich and Kurzrock feel that this need to maintain hope must be recognized and, if present, justifies early investigational drug treatment *regardless of the chance of tumour response.* Maintaining this hope, they further argue, may improve their quality of life.[26]

In response to this position, Schapira et al argue that this problem is often compounded by the failure of physicians to adequately communicate vital prognostic and therapeutic issues to such patients and by their inability to cope with their fear that refusal to offer investigational drugs would be perceived as removing hope. These authors suggest that providing access to early palliative care, rather than investigational drugs, offers an opportunity to maintain *a different kind of hope*. It is the hope of avoiding undue toxicity and of fulfilling life tasks that they consider important as their lives draw to a close.[27] Failure to help patients prepare for death deprives such a patient and loved ones of meaningful interactions while the patient remains free of treatment-related problems. Inner peace comes with adequate preparation for death, not creating a delusion that it will not come.

Coming to terms with a prognosis of imminent death involves a complex interplay between one's personal spiritual beliefs about life and death as well as one's personality, maturity of coping skills, and the adequacy of social support. Thompson et al insightfully suggest that open communication is important between terminally ill patients, their caregivers, and their supporting loved ones. It is also important to distinguish a patient's self-awareness of terminal illness and the acceptance of impending death. Appreciating this distinction can help to discern when patients accept the normative process of dying and when such patients may need help in understanding and coping with both death and its meaning for their life.[28] Studies have shown that discussing imminent death with a patient does not necessarily lead to hopelessness, despair, and depression, but rather to the patient spending more time at home or in hospice in order to become at peace with the ultimate affliction that each human being will face.[29] There is some evidence that patients who overestimate their prognosis receive more chemotherapy and more often die in hospital, yet do not live longer.[30] While Freireich and Kurzrock claim that discussions about palliative care are synonymous with or lead to despair and hopelessness, Schapira et al argue that hope is better understood as a dynamic expression of each person's humanity within its own rich and vital complexity.

The complexity of dealing with terminal illness is made even more complicated when the patient in question is a child and the parents must assume a role as surrogate decision-makers. In such cases, physician-investigators have an even greater responsibility to communicate benefits and risks clearly, honestly, and with some awareness of the parents' values and basic beliefs. In one recent study that surveyed parents of children who died of cancer a year or more earlier, investigators found that when parents understood that their children had no realistic chance of cure with chemotherapy, their expectations of cure dropped from 85% to 20%.[31] Twenty-two percent still harboured a goal of life extension while another 20% hoped that chemotherapy would at least lessen their child's suffering. Thus, helping these parents appreciate the increasing futility of treatment at some point led to major changes in expectations. Among parents whose child had participated in one or more phase I trials, 38% stated they would or probably would recommend experimental chemotherapy to another family. This decision was heavily influenced by whether or not their own child had suffered from participating in such a trial. The authors conclude that, when considering the use of chemotherapy in non-curative situations, physicians need to continue helping parents accept realistic expectations of therapy but also understand the risks of their child suffering due to the treatment itself. Physicians must also be aware that when two parents are involved in the decision-making process, one may perceive cure as the primary goal of chemotherapy while the other might see chemotherapy as a means

of providing palliative care. Other studies have reported the importance of clinicians identifying and supporting parents' faith practices as a means of helping parents cope and helping parents guide the spiritual welfare of their child.[32]

Such contrasting views on hope and approaching death demonstrate the continued challenges to end-of-life care and typify the different worldviews that encompass different views of human dignity and the role of death in life. As Schapira et al testify, patients find the strength to bear their illnesses, yet caregivers and loved ones may fail to realize that giving comfort and support add to that strength more than unproven therapies. Focusing on symptom assessment and relief, realistic outcome goals, and honest communication will provide more good care to most patients in that setting.

There is a need to have more discussions among Christian caregivers, patients, and their supporting persons to share biblical insights into advising patients regarding requesting investigational drug treatment in early phase testing. A view of death as the end to this life but also a beginning of new life can be part of an honest discussion if patients feel it would help them in their struggle with death and in formulating their own views which they may wish to better understand and articulate when given the chance.

In my view, a Christian ethical position on approaching patients for participation in clinical trials would require honest uncertainty on the part of the investigator about the efficacy, and less so the safety, of a new drug that should be communicated to patients who might be interested in enrolling into clinical studies. Patients should not have access to experimental drugs outside of participation in clinical trials at the end of phase I testing, given lingering uncertainty about safety even after Phase I testing and the complete lack of valid efficacy data. Similarly, phase II trials are meant to look for hints of efficacy that may or may not be later shown to be real. At this phase, confounding factors, such as having no contemporaneous control group or too few patients, make reliable conclusions about efficacy questionable at best. Furthermore, efficacy outcomes used in phase II studies, such as tumour shrinkage, are poor predictors of meaningful extension of life. For these reasons, justifying compassionate access after phase I or Phase II testing is very problematic. Given the slow pace of formal approval after completion of phase III trials and the presentation of positive results at medical conferences, access could be justified if the evidence was convincing and the only reason for unavailability the slow pace of formal regulatory approval. However, regardless of the phase of development, patients who participated in a clinical trial and experienced some level of benefit could also be considered for retreatment off-study if further benefit was judged to be possible.

As mentioned earlier, efforts are underway to identify biomarkers that may select patients who have a greater likelihood of deriving benefit from experimental drug treatment. Such biomarkers often represent therapeutic targets against which the drug has been developed. There is evidence that some drugs developed against such targets may improve patient outcomes by causing long-term stabilization of disease and longer remissions. The use of such identifying biomarkers could result in fewer patients receiving a drug off-study and outside of clinical trials via compassionate access. Patients eligible for phase II and III studies may require testing positive for the biomarker and more patients with the biomarker may enroll in studies if there is a greater chance of benefit. Furthermore, patients without the marker are often very unlikely to benefit and may not be offered the option due to the very low likelihood of benefit. However, there would still

remain the problem of patients refusing participation in phase III trials if they run the risk of not being randomized to a group receiving the study drug.

Most importantly, caregivers and patients must have a trusting relationship and honest discussions about caring for symptomatic, social, emotional, and spiritual needs as the futility of further anti-disease therapy becomes evident and is accepted. Taking time to care for those needs and sharing insights into the meaning of life and of death will constitute true care for patients at such a point near the end of life.

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# A Lutheran Defense of the HPV Vaccine

THOR SWANSON, MD

## Abstract

*Over the course of the last 7 years there has been considerable debate in the media, the public, and especially in the Conservative Protestant and Catholic communities over the appropriateness of the fairly new Human Papilloma Virus (HPV) vaccine. For instance, this author attended a Christian bioethics meeting in 2009 at the Center for Bioethics and Human Dignity in Chicago where a paper was presented against not only the mandatory use of the HPV vaccine, but any use of it at all.[1] Two years later, the value and ethical appropriateness of the vaccine resurfaced in a televised Republican presidential debate in Iowa on September 7th, 2011 in a heated interchange between presidential candidates Rep. Michelle Bachmann and Governor Rick Perry.[2] And finally, in October 2011, this author walked in on a discussion at a local food establishment between his wife and two of her middle aged female friends about the HPV vaccine. The conversation started because one of these friends told his wife and the other friend that she and her husband could not agree about whether to give the HPV vaccine to their pre-teen daughter or not. The mother, a college-educated women's studies major from Duke University, strongly supported giving her daughter the vaccine, but her politically and religiously conservative Lutheran husband was opposed.[3] Both official and unofficial debates over the HPV vaccine have occurred in the last 7 years in schools, physician offices, churches, and homes across the country. As a response to these ongoing national debates, this paper proposes support for the HPV vaccine in the United States based on a Lutheran bioethical analysis.*

## Medical Background

The medical discovery of vaccines has been a minor miracle for the modern human race. Childhood diseases, such as diphtheria, tetanus, and polio, which once wiped out families, neighborhoods, and tribes have been largely forgotten by the public in a day when few Western children die from these once formidable medical foes.[4] Although no one can say for sure, it is probable that thousands, or even millions, of children have been saved by such vaccines developed in the 20th century.[5]

The targets of the new HPV vaccines are the human papillomaviruses (HPVs). Although over 100 different genotypes of the HP virus have been discovered, only a smaller subset of these have been associated with human cancers.[6] Although there are several high risk HPV genotypes, HPV-16 is the most common, being found in more than 50% of cervical cancers worldwide.[7] The second most common cancer-related subtype is HPV-18.[8] Together, HPV-16 and HPV-18 account for about 70% of worldwide cervical cancer and an even higher proportion of other HPV-related cancers.[9] It is thought that both HPV-16 and HPV-18 contribute to cancer by inactivating innate P53 and RB tumor suppressor proteins that normally protect native cells from the rise of new cancers.[10]

Cervical cancer in women has been a plague on the human race for generations. As recently as 50 years ago, cervical cancer was the leading cause of cancer deaths in woman in the United States, but the mortality rate has since dropped by about 2/3 to its current

rate and current rank as the eighth leading cause of cancer death in women.[11] Much of the credit for these substantial improvements in the US has been the effectiveness of pap smear screening and subsequent colposcopy and biopsy of suspicious gynecological areas.[12]

What is the current prevalence and incidence of cervical cancer? On January 1, 2008 there were approximately 243,884 women alive in the United States who had a history of cancer of the cervix.[13] In 2013, an estimated 12,340 women will be newly diagnosed with cervical cancer and 4,030 women will die of cervical cancer.[14] From 2004-2008, the median age of diagnosis for cancer of the cervix uteri in the US was 48 years of age[15] and the median age of death for cancer of the cervix was 57 years of age.[16] The HPV vaccine lends promise to the fight against cervical cancer as HPV DNA is detected by hybridization techniques in over 95% of cervical cancers and specific HPV types targeted by the vaccine are associated with a high risk of cervical cancer.[17]

Anal cancer too continues to be a problem for both men and women. In 2013, a projected 7,060 men and women will be diagnosed with cancer of the anus, anal canal, and ano-rectum and 7,880 men and women will die of the same.[18] The HPV vaccine lends promise in these situations as well, as HPV DNA is also linked with a high risk of anal cancer.[19] In particular, HPV-16 has been found to have a high degree of association with anal squamous cancer, as to a lesser degree have types 18, 31, 33, 35 and others.[20] In some published series, these high-risk HPV types have been found in 85% of anal squamous cancers.[21] This issue especially impacts the gay male population, which has a higher rate of anal cancer due to HPV infection acquired in anal sex.[22]

And finally, HPV has been long thought to have a link to head and neck cancers. In 2013, somewhere around 12,260 men and women will be diagnosed with new laryngeal cancer and 13,930 with new pharyngeal cancers.[23] Further, there will be about 3,630 deaths from laryngeal cancer and 2,400 deaths from pharyngeal cancer.[24] While earlier studies (closer to 20 years ago) found HPV to be detected in about 25% of these cancers,[25] the association is thought now to be closer to 70%.[26] Again, the HPV subtypes found in these cancers has overwhelmingly included the oncogenic ones, especially HPV-16.[27]

Besides these three key groups of cervical, anal, and head and neck cancers, HPV has also been shown to be associated with cancers of the vulva, vagina, and penis.[28]

A first vaccine that protects against Human Papilloma Virus infection, manufactured by Merck and marketed as Gardisil, was approved by the FDA in June 2006.[29] This vaccine is administered in 3 doses over a 6 month period and is intended to protect against HPV subtypes 6, 11, 16, and 18. A second vaccine manufactured by GlaxoSmithKline and entitled Cervarix was approved by the FDA in October 2009.[30] This second vaccine only protects against HPV subtypes 16 and 18 and is also administered in 3 doses over a six-month period. The HPV debate focuses on the recommendations of the Centers for Disease Control and Prevention and other health bodies to vaccinate 11 and 12 year old girls with 3 doses of the vaccine.[31] The HPV vaccine is also recommended for girls and women ages 13 through 26 who did not get any or all of the doses when they were younger, and should be available to boys and men ages 9 through 26.[3]

## General Bioethical Principles

A proper defense of the HPV vaccine begins with the four principles of bioethics that have dominated Western Medical Ethics for the last 40 years: beneficence, non-maleficence, justice and autonomy.[33] While Lutheran medical ethics will embrace something more than just these four principles, it certainly includes them as a starting basis of discussion. [34]

Like all vaccines, the HPV vaccine is an attempt at beneficence (doing good). Seeing the cancers caused by HPV virus, researchers hypothesized that control of HPV could limit cancers, and this insight led the development of the vaccine. Today, the vaccine seeks to protect mostly women, but also men (especially gay) from cancer. The goal of "doing good" with this vaccine must not be doubted, as extensive testing has showed that the vaccine does drop the rate of cancer in those immunized. For instance, clinical trials showed that Gardisil had both a 100% efficacy in preventing cervical pre-cancers caused by the targeted HPV viral subtypes and a nearly 100% efficacy in preventing vulvar and vaginal pre-cancers and genital warts caused by the relevant HPV subtypes (among women ages 16 to 26 who were previously uninfected by the subtypes).[35] Information on the high efficacy of both these vaccines is available from the CDC and FDA websites.[36]

The HPV vaccine protects against cancer. If it did so at a price, namely by producing bad side effects, the vaccine could be questioned on the basis of doing no harm (non-maleficence). The most common side effects, however, are pain and redness where the shot is given (in the arm). About 1 in 10 vaccinated persons will get a mild fever. About 1 in 30 vaccinated individuals will get itching at the injection site. About 1 in 60 given the shot will experience a moderate fever. Alleged serious reactions are rare. While there have been deaths attributed to the HPV vaccines in the press and reported to the Vaccine Adverse Event Reporting System, as the CDC website states, "all reports of death are reviewed by medical doctors or the CDC or FDA… there have been no patterns of deaths reported that would suggest they were caused by the vaccine."[37] The safety of the vaccines was studied in clinical trials prior to FDA approval and continues to be monitored by the CDC. Overwhelmingly, the vaccine has been shown to be safe and the CDC continues to declare it so.[38] The vaccine accomplishes its good (see above) with little or no problems (non-maleficence) in terms of side effects.

Some moral opponents of the vaccine claim the vaccine does harm (maleficence) by encouraging teenagers to engage in unsafe sex practices.[39] From 2006 until 2012, proponents on both sides of the HPV vaccine question speculated about what data would eventually show about HPV and the onset of subsequent sexual activity in teenagers. Finally in fall 2012, the first study following the subsequent sexual behavior of immunized children was published. The research followed 1,398 girls who received the vaccine as 11 or 12 year olds between July of 2006 and December of 2007 in the Atlanta, Georgia metropolitan area and tracked the sexual activity of these young women through the use of clinical records over the subsequent three years, cutting off at the end of 2010. The result was, as the conclusion states, that "HPV vaccination in the recommended ages was not associated with increased sexual activity-related outcome rates."[40]

This first study from Atlanta, Georgia does not, of course, guarantee that all future studies, in different ethnic groups, locales, and situations will duplicate the same results. However, the clinical experience of this author believes most or all these futures studies will reinforce little or no relationship between the HPV vaccine and subsequent sexual activity. In his own informal surveys of teenage girls seen in his own multicultural,

multi-ethnic clinic, low-income family medicine clinic in Sioux City, IA, the author has found very little awareness of the HPV virus, the HPV vaccine, the link between the HPV virus and cervical cancer, or the link between HPV and sexually transmitted diseases in adolescent girls or even young women. Many published studies of adult woman and teenage girls have shown woefully low public knowledge in many places of these issues related to the HPV vaccine.[41] In order for the HPV vaccine to lead to increased sexual activity, the immunized adolescent would have to make a series of connections in her/his brain that include—the HPV virus exists—the HPV virus is an STD that causes cervical cancer—the HPV vaccine exists, which decreases my risk of cervical cancer—therefore I don't have to be so afraid of sex and I will become sexually active. The knowledge basis in adolescents just doesn't exist to make those connections and lead to increased sexual activity.

The argument of the vaccine opponents seems to imply that teenagers or young adults will go out and become sexually active, or be more likely to be sexually active, if they know they are protected from HPV and cervical cancer. However, as even conservative Christian policy analysts note, teenagers continue to be sexually active in the wake of high teenage STD rates (each year 25% of sexually active teens acquire an STD; about 25% of all new cases of STDs occur in teenagers) and the potentially fatal virus of HIV.[42] If these situations fail to stop teenage sex, should one really expect that the possibility of HPV–associated complications somewhere down the road will curb teens' choices with regards to sexuality either? Even some social conservatives are realizing the argument against the vaccine probably needs to be abandoned.[43]

Universal vaccination for HPV in the United States is also an attempt at justice, especially towards those who are poor and don't have equal access to medical resources. In the United States, a recent study showed that lower education and higher poverty were found in the United States to be associated with increased penile, cervical and vaginal invasive cancer rates.[44] Further, rates of HPV-associated cervical cancers are nearly twice as high in poorer counties of the United States compared to rich ones.[45] The causes of these associations have not been quantified, but probably include exposure risk, preventative diagnostic screening, or other variables.[46] Universal vaccinations will protect all alike from the virus and cancers, but especially the poor of the US who are disproportionately affected by HPV.[47]

In the end, from the standpoint of beneficence, nonmalficence, justice, and autonomy, Lutherans should support the HPV vaccine.

## Lutheran Distinctives

Throughout the 2,000-year history of Christianity, the majority of Christian denominations and sects have supported the role of physicians, nurses, hospitals and medicines in both preserving health and treating disease.[48] Lutherans have been one of those denominations, encouraging the role of health authorities in promoting human health.[49]

A Lutheran[50] defense of health care can be two-fold, rooted in both aspects of theology, Law and Gospel.[51] For Lutherans, the Law includes God's demands, his commands for human people. The Law also includes both eternal moral commands, which are meant for every time and every place, and provisional commands, meant only for a selection time or dispensation.[52] For Lutherans, the Gospel entails the actions and promises that God does for people, securing their redemption and restoration. For Lutherans, Jesus' actions in

emptying himself of divine glory, taking on human flesh, ministering in a broken world, dying on the cross for sins, and rising again to show his power over death all constitute the Gospel.[53]

Lutherans have historically been consistent in saying that the command to love one's neighbor is part of the moral law, commanded to non-Jewish inhabitants of the world before Christ, Jewish followers of God in the world before Christ, and Christians living after Christ.[54] Other elements of the universal moral law generally accepted by traditionalist Lutheran Christians have included the duty to promote life and avoid murder, to avoid theft and labor, to avoid lying and speak truthfully, to avoid extra-marital infidelity and promote intra-marital love and faithfulness.[55]

Physicians, nurses, therapists and pharmacists who participate in health care and aid sick people are, from the Lutheran point of view, fulfilling the Law by loving their neighbor—they are doing God's work, whether they realize it or not. Such health care providers are God's agents of healing and wholeness, and Lutherans call this the doctrine of vocation.[56] God's rule, God's kingdom is coming to the world through such people, whether or not they actively follow God or go to church.[57] Medicines, vaccines, therapies, hospitals, intricate radiology machines, and laboratory machines are all tools that God has provided for health care providers to exercise their health care vocation. They are all blessings with which the medical provider may become a blessing has to others and uphold the love of neighbor. Although the Old Testament apocryphal work, The Wisdom of Ben Sirach, is not part of the Lutheran canonical scriptures, the Lutheran agrees with the writing, "Make friends with the physician, for he is essential to you; him also God has established in his profession. From God the doctor has his wisdom… God endows humans with the knowledge to glory in his works, through which the doctor eases his pain and the druggist prepares his medicines; Thus God's creative work continues… on the surface of the earth." (Wisdom of Ben Sirach, 38:1-8)[58]

The medical physician has a multitude of tasks in his vocation of provider, including prevention of new disease and treatment of ongoing illness. Emphasis on the first, as all health care studies show, saves time, money, and effort on the second task. One key element of prevention of disease includes vaccines like HPV. In the eyes of Lutheran medical practice, the HPV vaccine, given in three doses to pre-teenage girls (and probably eventually boys also), does and will prevent disease, which is part of caring for the neighbor's health. From this standpoint, the vaccine should clearly be supported because this is one of many ways that the doctor, nurse, and health care workers fulfill the Law by loving their neighbor.

While Lutherans have always recognized even non-Christians as participating in the vocation of healing, an argument can also be made for the vaccine from the Gospel. In reading the Gospels of the Christian scriptures, healing from sickness and death were fundamental to the ministry of Jesus.[59] Jesus' actions in healing people were Gospel, Grace, and Good News for people, in the Lutheran sense. For that reason, Lutherans have always seen Christian participation in the healing ministries as appropriate and, even more than that, a true Christian service. Christians may not have the same power as Jesus, the second person of the Trinity, to lay hands on people and make them instantly better by their own power, yet Lutherans recognize that being a vehicle in God's healing is a great demonstration of Christian discipleship. The opportunity to be a vehicle of God's

healing of the sick, allows Christians to imitate, in a small way, the life and ministry of their savior Jesus. Offering pre-teen children the HPV vaccine does the same.

Some opponents of the HPV vaccine stand against it on moral grounds. They suggest that using the HPV vaccine will encourage inappropriate sexual practices (sin) and contribute to immorality (see above). Even if that could be proven, it still would not seal the case against the vaccine from a Lutheran perspective. Lutherans have long recognized that involvement with the world will involve Christians in difficult moral situations. As opposed to some Protestant Christian groups, who withdraw from the world to avoid difficult moral choices (the Mennonites), or others that try to take over the world to avoid them (the Reformed tradition), Lutherans have longed occupied a middle ground between these two extremes that advocates neither retreat nor conquest, but rather engagement. In his now classic, *Christ and Culture*, H. Richard Niebuhr entitled this form of social ethics "Christ Restraining Culture."[60] Others have entitled this method, as taught by Richard's more Lutheran brother Reinhold Niebuhr, "Critical Realism."[61]

Lutheran critical-realism recognizes the fallen-ness of the world in its current state, but also claims that Christians can neither abandon it, nor expect to ever improve it much. This approach assumes that every day the citizens of God's world will make bad choices which lead to bad consequences; however, in faithfulness to neighbor, the Lutheran still sees a Christian call to love his or her neighbors and try to improve their lives anyway.[62] Lutherans may not affirm extra-marital sexual activity, but if people are going to engage in such activity anyway, Christians still have a moral duty to try to help them stave off the bad consequences of that choice. Also, just because someone is going to have pre-marital or extra-marital sex does not mean Christians are morally justified in not telling them about STDs (Chlamydia, Gonorrhea, HIV, HPV, Herpes) and their outcomes. The Lutheran critical-realist recognizes that sometimes there is not a good choice, just a less bad choice. While the world would be a better place with lifelong monogamy, no rape, and only one life sexual partner, Lutheran critical-realism realizes that scenario will not occur until the arrival of the New Heaven and the New Earth. In the meantime, using HPV to control cervical cancers, anal cancers, warts, and other sequelae is clearly a good, or at least a lesser evil than doing nothing.

Some proponents of the vaccine claim that it should be mandatorily required and enforced against recalcitrant parents and teens.[63] As many have noted, if parents are morally opposed to the vaccine, and a child, especially a girl, is not vaccinated, she may be exposed to the HPV virus through sex (whether it be willfully chosen or through rape) and destined for its complications[64] before she reaches an age (18) when she can willfully choose the vaccine against her parent's wishes. They claim that society reclaims the duty to vaccinate children, especially girls, against the virus before they are tragically exposed. These proponents of mandatory vaccination make the point that protection/defense of that neighbor does include the HPV vaccine. However, the Lutheran bioethicist also will realize that many of those parents are doing their best to love their children and fulfill their vocation as parents.[65] The Lutheran bioethicist should not agree with the parents' decision, but must affirm the parents' desire to defend their child. Again, for the Lutheran critical-realist there is no exactly right answer in affirming the parent's choice against the good vaccine or enforcing the vaccine and undermining the parent's role and vocation. Given the fact that the HPV vaccine does not provide an immediate threat to the child's health, such as the Jehovah's Witness child who must get a blood transfusion or die,[66] Lutherans should support voluntary rather than mandatory vaccination. Nevertheless, Lutherans

should also encourage anti-vaccinationist parents to continue an ongoing discussion about the vaccine with their doctors, spiritual leaders, and community acquintances.[67] A non-mandatory approach is the lesser of two evils in this case.

## Conclusion

This paper has examined the HPV vaccine through the lens of both common Bioethical principles and specifically Lutheran theological lenses. In each case, the voluntary use of the vaccine has been affirmed. Of course, Christians of other theological schools and non-Christians may continue to disagree with this approach and raise objections.

## Endnotes

1. As of Fall 2012, the Center For Bioethics and Human Dignity website had a paper available online against the vaccine. See there the article by Susan Haack, "HPV Vaccine: Panacea or Pandora's Box? The Costs and Deceptiveness of the New Technology," available at http://cbhd.org/content/ .
2. One of many articles available on the web is "Michele Bachmann links Rick Perry on HPV vaccine to Solyndra" from the *Los Angeles Times*, dated September 16, 2011. It is available at http://articles.latimes.com/print/2011/sep/16/news/la-pn-bachmann-costa-mesa-20110916 .
3. And since this time, the author, a family practice physician, has been involved with many different religious parents with varying convictions about the vaccine, the majority being skeptical.
4. For a very readable account of the history of some of these diseases and vaccines see Michael B. A. Oldstone, *Viruses, Plagues and History: Past, Present, and Future*, Revised and Updated Ed., (New York: Oxford University Press, 2010).
5. See the above book *Viruses, Plagues and History* for success stories of many viral vaccines.
6. Devita, Vincent T., Theodore S. Lawrence, and Steven A. Rosenberg, eds., *DeVita Hellman and Rosenberg's Cancer: Principles and Practice of Oncology*, 8th ed., (Philadelphia: Lippincott, 2008), Vol 1., p. 552.
7. Ibid.
8. Ibid.
9. Ibid.
10. Ibid.
11. Kumar, Vinay and Abul, Abbas. Nelson Fausto, and Jon Aster, editors. *Robbins and Cotran Pathologic Basis of Disease*, 8th Ed., (Philadelphia: Saunders, 2010), p. 1018.
12. Ibid.
13. See information from the National Cancer Institute at www.cancer.gov/cancertopics/types/cervical .
14. Ibid.
15. Ibid.
16. Ibid.
17. See *Robbins and Cotran Pathologic Basis of Disease*, 7th ed., (Philadelphia: Elsevier), p. 1074.
18. See information from the National Cancer Institute at www.cancer.gov/cancertopics/types/anal .
19. See for instance the paper by J. R. Daling, M. M. Madeleine, L. G. Johnson, et al. "Human Papillomavirus, Smoking, and Sexual Practices in the Etiology of Anal Cancer" in *Cancer*, 2004, 101:281-288.
20. Devita, et.al., *Cancer*, Vol. 1, p. 1303.
21. Ibid.
22. See Daling et al, "Human Papillomavirus." For instance, in our small, rural HIV clinic in Iowa, we have seen several cases of anal cancer amongst our HIV positive, gay male patients.
23. See projections from the National Cancer Institute at www.cancer.gov/cancertopics/throat .

24. Ibid.
25. Devita et. al, *Cancer*, Vol. 1, p. 805.
26. See information from the National Cancer Institute with references at www.cancer.gov/cancertopics/types/throat .
27. Devita et al., *Cancer*, Vol. 1, p. 805.
28. See information on these cancers from the National Cancer Institute at www.cancer.gov/cancertopics/types.
29. Detailed information about the Gardisil vaccine is available on the FDA website at http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm094042.htm .
30. Detailed information about the Cervarix vaccine is available on the FDA website at http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm186957.htm .
31. Not only the CDC, but the American Academy of Pediatrics has endorsed these recommendations. See the Centers For Disease Control information about HPV at http://www.cdc.gov/vaccinesafety/Vaccines/HPV/hpv_faqs.html .
32. Ibid.
33. For a general discussion of these principles, see especially Tom L. Beauchamp and James F. Childress, *Principles of Biomedical Ethics*, (New York, Oxford University Press, 2009). For an example of how these principles can be used in the HPV debate see Robert I.Field and Arthur L. Caplan, "A Proposed Ethical Framework for Vaccine Mandates: Competing Values and the Case of HPV" in *Kennedy Institute of Ethics Journal*, Volume 18, Issue 2, June 2008; pages 111-124.
34. As Lutheran bioethicist Gilbert Meilaender rightly notes in *Bioethics: A Primer For Christians* (Grand Rapids: Eerdmans Publishing House, 2005), 2nd edition, p. 1.
35. See the product information for Gardisil and Cervarix available at the FDA website at http://www.fda.gov.
36. See the information on HPV vaccine safety at the CDC website at http://www.cdc.gov/vaccinesafety/Vaccines/HPV faqs.html .
37. See the information on HPV vaccine safety at the CDC at: http://www.cdc.gov/vaccinesafety/Vaccines/HPV/hpv_faqs.html.
38. Ibid.
39. As for example Bridget Maher of the Family Research Council in 2005 as noted at http://findarticles.com/p/articles/mi_qa3944/is_200507/ai_n14824000/ .
40. See Robert A. Bedarczyk, Robert Davis, Kevin Ault, Walter Orenstein and Saad B. Omer. "Sexual Activity-Related Outcomes After Human Papilloma Vaccination of 11- to 12- Year Olds", *Pediatrics*, 2012, 130:798-805).
41. See for instance the study by K. Fazekas, N. Brewer, and J. Smith, "HPV Acceptability In A Rural Southern Area", in *Journal of Women's Health*, 2008, 56:1-24) which showed that only 36% of 149 girls and women ages 13 to 26 at a rural southern clinic had heard about HPV and only 19% had heard about a vaccine.
42. See Bridget Maher, "Abstinence Until Marriage: The Best Message for Teens" at http://www.lifeissues.net/writers/mah/mah_01abstinenceteens.html .
43. See for instance the piece by Diane Ellis entitled "Rick Perry, Social Conservatives, and the HPV Vaccine" available at: http://ricochet/com/main-feed/Rick-Perry-Social-Conservatives-and-the-HPV-Vaccine .
44. See Vicki B. Benard et al., "Examining the Association Between Socioeconomic Status and Potential Human Papillomavirus-associated Cancers" in *Supplement to Cancer*, pp. 2910-2918, published in 2008 by the American Cancer Society.
45. See the information on HPV and poverty at the CDC at: http://www.cdc.gov/cancer/hpv/statistics/poverty.htm .
46. Benard et al., "Examining", *Supplement to Cancer*, pp. 2916ff.
47. This paper does not examine the moral argument for using the vaccine in the 3rd world where poverty and other issues lead to high rates of cervical cancer. In those settings, unique cultural factors such as religion, access to medical care, etc. will need to be examined further.
48. See for instance Amanda Porterfield, *Healing in the History of Christianity* (New York: Oxford

University Press, 2005).

49. For a general discussion of Lutherans and medicine see Martin E. Marty, *Health and Medicine in the Lutheran Tradition: Being Well*, (New York: The Crossroad Publishing Company), 1983. For a historical overview of Lutherans and medicine see Carter Lindberg, "The Lutheran Tradition" in *Caring and Curing: Health and Medicine in the Western Religious Traditions*, (Baltimore: The Johns Hopkins University Press, 1986), pp. 173-203.
50. And, for that matter, the Reformed tradition. The Lutheran and Reformed traditions operate quite similarly on these issues.
51. For the place of Law and Gospel in the theology of Martin Luther see Robert Kolb and Charles P. Arand, *The Genius of Luther's Theology*, (Grand Rapids: Baker Academic Press, 2008). For the place of Law and Gospel in Lutheran bioethics see Richard C. Eyer, *Holy People, Holy Lives: Law and Gospel in Bioethics*, (St. Louis: Concordia Publishing House, 2000).
52. For a discussion of the Law in a Lutheran Systematic Theology see John Theodore Mueller, *Christian Dogmatics.* (St. Louis: Concordia Publishing House, 1955), esp. pp. 479ff., and in the works of a Lutheran bioethicist see Eyer, *Holy People*, esp. pp. 61ff.
53. For a discussion of the Gospel in a Lutheran Systematic Theology see Mueller, *Christian Dogmatics*, esp. pp. 470ff. and in the works of a Lutheran bioethicist in Eyer, *Holy People*, esp. pp.66ff.
54. For aspects of the natural law in the Lutheran confessions, Lutheran theology and Lutheran history, see especially Robert C. Baker and Roland Ehlke, eds., *Natural Law: A Lutheran Appraisal*, (St. Louis: Concordia Publishing House, 2011).
55. See the extensive discussion by Lutheran bioethicist Gilbert Meilaender, *The Freedom of a Christian: Grace, Vocation, and the Meaning of our Humanity* (Grand Rapids: Brazos Press, 2006), especially chapter 2.
56. For an introduction to Martin Luther's doctrine of vocation see Gustaf Wingren, *Luther on Vocation* (Philadelphia: Muhlenberg Press, 1957). For a recent Lutheran reflection on vocation see Gene Edward Veith, Jr., *God At Work: Your Christian Vocation In All Of Life* (Wheaton: Crossway Books, 2002).
57. See Gustaf Wingren, *Luther On Vocation*, (Philadelphia: Muhlenberg Press, 1957) and Gene Edward Veith, Jr., *God At Work: Your Chrisitian Vocation In All Of Life* (Wheaton: Crossway Books, 2002), esp. pp. 17ff.
58. For a detailed discussion of this passage, see Patrick W. Skehan, *The Wisdom of Ben Sira* in the Anchor Bible Series (New York: Doubleday, 1987), esp. pp. 438-444.
59. See the reflections of Lutheran minister and medical anthropologist Garth D. Ludwig in *Order Restored: A Biblical Interpretation of Health Medicine and Healing*, (St. Louis: Concordia Publishing House, 1999).
60. See H. Richard Niebuhr, *Christ and Culture*, 50th anniversary edition (San Francisco: Harper and Row, 2001).
61. For a brief introduction to Reinhold Niebuhr and his Lutheran-style critical realism see, Robin W. Lovin, *Reinhold Niebuhr* (Nashville: Abingdon Press ,2007).
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63. For an early discussion of the ethics and politics of mandatory HPV vaccination see James Colgrave, "The Ethics and Politics of Compulsory HPV Vaccination" in *New England Journal of Medicine*, 2006, 355: 2389-2391, December 7, 2006. For some of the arguments used by those seeking to make the vaccine mandatory see C. A. Vamos, R. J. McDermott, and E. M. Daley, "The HPV Vaccine: Framing the arguments FOR and AGAINST mandatory vaccination of all middle school girls" in *Journal pp. of School Health*, 78(6): 302-309, June 2008. For an article discussing the controversy surrounding a mandatory HPV vaccination program see, James Colgrave et. al., HPV Vaccination Mandates-Lawmaking amid Political and Scientific Controversy" *in New England Journal of Medicine*, Vol. 363, number 8, August 19, 2010, pp. 785-791.
64. As, for instance, noted on the *First Things* editorial page by Christopher Kaczar, "Christian Parents and the HPV Vaccine" on June 2nd, 2011 at http://www.firstthings.com/onthesquare/2011/06/christian-parents-and-the-hpv-vaccine .

65. For a discussion of the Lutheran doctrine of vocation in the family see Veith, *God At Work*, 77ff.
66. See, for instance, the discussion of ethical issues in pediatrics in Bernard Lo, *Resolving Ethical Dilemnas: A Guide For Clinicians*, 4th ed., (Philadelphia: Lippincott, 2009), pp. 267-277.
67. For instance, Lutherans should affirm exactly the kind of discussion the author walked in on between three women in a food establishment as noted in the introduction.

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# Playing God: Medical Ethics and Biblical Justice

*An Address to the McWhorter School of Pharmacy Samford University, April 11, 2011*

MATTHEW S. KERLIN, PHD

## Introduction

My initial interest in medical ethics stems in part from an experience involving a medication error. My younger brother was born with a cardiac anomaly known as Tetralogy of Fallot, a condition involving a variety of defects ranging from mild to life threatening. While being treated for this condition in 1985, he was accidentally administered the wrong medicine by a young nurse who, realizing her error, panicked and told no one. My brother's condition worsened and several weeks later he died. Perhaps he would have died anyway, and perhaps not. We will never know, which is probably why my parents chose never to file suit, a decision we have never regretted. My brother's death, and the circumstances surrounding it, awakened me from the dreamy innocence of childhood and forced me, for the first time in my life, to think long and hard about life's complex mix of beauty and pain. I later married a nurse who works in labor and delivery and probably knows more about beauty and pain than anyone I know. I now get paid to work with students in the midst of life's complex mix of learning and struggle. And, thus, a theological journey that began with a medication error has brought me to write about playing God, medical ethics, and biblical justice. Let me discuss each of the three in turn to see how they relate to one another.

## Playing God

First, a disclaimer: I am a theologian, so when I think about ethics I do so with consideration of how beliefs influence decisions. What we think about God often affects how we act toward one another. Some of my research in this area has involved examining how the rhetoric of "playing God" has shaped ethical decision-making in medicine.[1] Take, for example, a question often associated with life and death decisions: "Who are we to play God?" The implications of the question by those who ask it are often these: (1) God alone is creator. (2) Ultimately, God gives life and God should decide when it ends. (3) As medical professionals, we should not take life, or hasten death, since to do so is God's job alone, or so the argument goes. Yet, many of the same individuals who would object to "playing God" in order to hasten death would not object to playing God in extraordinary ways to lengthen life. Do we not play God when we take a heart out of a dead person and place it inside the body of a dying person? Or when an infant born 3 months prematurely survives after 3 months of round-the-clock intensive care? Or when we inject chemicals into the veins of a cancer patient, chemicals so toxic that if touched they could make the one administering them sick? The truth is, we play God all the time. And when our lives or the quality of our lives are threatened, we want someone to play God on our behalf.

This reality takes center stage in the 1993 movie *Malice* starring Alec Baldwin, who plays the role of Jed Hill, a talented trauma surgeon. Following a surgical procedure that

goes badly, Hill is deposed by attorneys who ask him point blank, "Do you have a God complex?" He responds with the following monologue:

> The question makes me wonder if this lawyer has any idea as to the kind of grades one has to receive in college to be accepted at a top medical school. Do you have the slightest clue how talented one has to be to lead a surgical team? I have an M.D. from Harvard. I am board certified in cardiothoracic medicine and trauma surgery. I have been awarded citations from seven different medical boards in New England. So I ask you, when someone goes into that hospital chapel and they fall on their knees and they pray to God that their wife doesn't miscarry, or that their daughter doesn't bleed to death, or that their mother doesn't suffer acute neural trauma from postoperative shock, who do you think they're praying to? Now, you go ahead and read your Bible, you go to your church, but if you're looking for God, here he is. You asked me if I have a God complex. Let me tell you something. I am God.[2]

The movie is crafted in such a way that, as viewers, we are simultaneously appalled by his arrogance and yet impressed by his confidence and his power to save life, in effect, to play God. We do not like him as a person, but we want him as a surgeon. If you have ever faced the sharp end of a scalpel, you have probably prayed and wanted a surgeon who can play God, and play the role well. The point is that while we may not always agree on playing God at the end of life, most people agree with the virtue of playing God to save life or to improve the quality of life. Which brings us to our next subject.

## Medical Ethics

Historically, medical ethics has involved extremely complex decisions that naturally invoke questions about playing God. Let me offer two brief examples, one classic ethics case and one recent hopeful scientific breakthrough, both of which force us to ask if we are, or should be, playing God.

First, the case of Karen Quinlan is still one of the most famous in American medical ethics. The issues raised by the case, in many ways, still haunt medicine today. In 1975, Quinlan, age 21, celebrated a friend's birthday at a local bar where she consumed several drinks before being taken home and put to bed by friends. Shortly thereafter she stopped breathing and lost consciousness but was resuscitated by a policeman and began breathing again. She did not regain consciousness, however, and was admitted to the intensive-care unit of a hospital in suburban New Jersey. Tests revealed a combination of alcohol and barbiturates in her bloodstream that doctors believed suppressed her breathing, causing irreversible brain damage. She was placed on a respirator and a feeding tube when she began to show classic signs of profound neurological trauma. Although she was given a one-in-a-million chance of recovery, she was not technically brain dead according to New Jersey state law. Consequently, when the Quinlan family decided that life-support should be removed, it took them nearly a year to obtain the legal right to do so. The hospital then refused to remove life support for an additional five months. When they finally did, Karen Quinlan began to breathe on her own. She lived in a persistent vegetative state for more than ten years.

Second, let us consider a recent scientific breakthrough. On April 6th of 2011 the BBC reported that the journal *Nature* planed to publish an article written by a team of Japanese scientists who used stem cells from a mouse to grow a synthetic retina. Ultimately, the scientists hope they can use this approach to make endless supplies of

retinal cells, or indeed whole retinas, that can be transplanted into patients with visual impairment. Eventually, the scientists believe, it may even be possible to create a whole eye. A US biotech company has already been granted a license to begin human trials of a stem cell treatment for blindness, believing that the "self-formation of fully stratified 3D neural retina tissues heralds the next generation of generative medicine in retinal degeneration therapeutics, and opens up new avenues for the transplantation of artificial retinal tissue sheets, rather than simple cell grafting."[3] Professor James Bainbridge of Moorfields Eye Hospital said, "The generation of a synthetic retina from embryonic stem cells is a landmark discovery that will help enormously our understanding of blinding eye disease."[4]

These two scenarios represent the history of discourse surrounding medical ethics in America, from its infancy in the 1970s, when hospitals were just beginning to form ethics boards to handle such cases, to the current debates over cloning, genetic engineering, and stem cell research that are almost too complex for all but professionals to understand. With respect to playing God, these two cases contain one glaring difference as well as one important similarity. Let us first consider the difference. The Quinlan story was major news for months. Volumes have been written about the case. Ethicists study it today and thousands of people have spent countless hours debating it. In contrast, the story about engineering synthetic retinas did not make the evening news, did not appear on the cover of any paper or magazine, was buried deep within my RSS feed online, and weeks from now, maybe even hours, few will even remember the discovery. Why? Because death is considered more newsworthy than life. Because while we fear playing God to hasten death, we give insufficient thought to playing God when it comes to engineering life artificially. To quote from the movie Jurassic Park, "we are in such a hurry to see if we can, that we rarely stop to ask if we should." It would be tempting at this point to follow this line of thinking and to discuss the circumstances in which one should, and should not, play God. Instead, I am going to follow a different path.

How are the scenarios similar? These two cases, and the ethical discourse they inevitably engender, are almost completely irrelevant for most of the world's population; irrelevant because access to sophisticated life-prolonging and life-improving technology is simply out of reach for most of the world. Let me repeat that. For most of the world's population, the discourse of Western medical ethics has been largely irrelevant because it concerns resources that are unavailable to the majority of people globally. Consider these statistics:

According to the World Bank's Development Indicators [2010]:

- 40% of the world's population lives on less than $2,000 a year
- 1 billion people survive on just $1 per day
- A $100,000 annual salary places you in the top .6% of the world's wage earners
- 830 million people go hungry each day (consuming less than 1800 calories daily)
- Over 32,000 children die from hunger daily
- 134 million children between 7-18 years of age have no formal education
- 30 million children have no immunization against preventable diseases
- 1.4 million children die annually from preventable diseases
- There are approximately 1.75 million sex slaves worldwide

- 40% of prostitutes in India and Thailand are children[5]

So scientists can now grow an eyeball in a petri dish. What relevance does this have for a child prostitute in Thailand who goes blind from syphilis? Our ethical conversations have been far more concerned with the proper use of technology than with equitable access to technology both here and abroad. Most advances in technology that lengthen and improve life come at a high price that most cannot pay. Deciding *how* to use sophisticated and expensive technology is the ethical conversation of a privileged people, and a worthy discussion no doubt. But deciding *who* benefits from such technology is the emerging ethical conversation of our time. This is where the biblical concept of distributive justice can be particularly helpful.[6]

## Biblical Justice

Here I should say that I know not everyone shares the same view of the Bible or its inspiration and authority for the life of faith. Still, I ask you to hear me out because I believe the Bible offers a critique of Western medical ethics that we all should consider. In the Bible, we find two types of justice, retributive justice and distributive justice. Retributive justice has to do with punishment or retribution, a classic expression of which appears in the Old Testament standard "an eye for an eye and a tooth for a tooth," and in the New Testament in Jesus' rejection of that standard.[7] Distributive justice, however, has to do with the fair distribution of resources. I have two sandwiches, you have none and are hungry, and so I give you one of mine. Contrary to popular perception, the Bible speaks as often about distribution as retribution, and the concept makes us uncomfortable.

When Barack Obama ran for his first term as president, he was often asked whether he believed in the redistribution of wealth in America. The question was divisive because so many are uncomfortable with the idea of government redistribution. Bear in mind, however, that the distribution about which the Bible speaks is not governmental, it is communal. Biblical distributive justice does not consist of money paid to a government so that elected officials can care for the poor. Distributive justice is about people living in such a way so that the extravagance of a few does not coexist with the misery of the many. Justice is about creating economic, religious, and social structures that sustain everyone so that everyone's needs are met. In other words, biblical justice is not fundamentally about re-distribution at all. It is about proper distribution in the first place. We sometimes equate justice with generosity or charity. Charity occurs when I have more than I need and I give some of it to someone less fortunate. Charity is not justice; charity is needed precisely because there is injustice. If perfect justice existed, there would be no need for generosity. The work of justice is about making sure that everyone gets a sandwich, so that I do not throw away what I cannot eat as others starve.

Throughout the Bible, God gives instructions intended to create systemic justice. Let me offer three examples: gleaning, tithing, and the Jubilee year. Leviticus and Deuteronomy specify that farmers were to leave the corners of their fields un-harvested. They were to leave a few grapes on the vine and a few olives on the tree, so that the poor and the foreigner could glean food to eat. Old Testament law also specifies that a tithe of one's income or produce be given to religious leaders who were to eat only what they needed and then distribute the rest to those in need. The Jubilee year is even more radical, so radical in fact that we have no evidence that the Israelites ever practiced it. Each seventh year, one's fields were to lay unplowed so they could rest, an agricultural Sabbath

of sorts. On the seventh of the seventh years (the 49th year), the land was to lay fallow, and amazingly, a horn was to sound signifying that all property was to be returned to its original owner, all debts were to be forgiven, and all slaves set free.

When I teach this concept to undergraduates, I ask them to imagine this situation: It is final exam week. You are in the library. It turns midnight and someone blows a horn and the university president announces that effective immediately, all exams are cancelled, everyone passes, tuition for the year is free, all school loans are forgiven, and all parking tickets are forgiven. No longer would banks, professors, parents, financial aid officers, or academic advisors have any power over you. In that moment, there would be radical, undeserved, unearned distributive justice.

Of course, I know what you are now thinking. Impossible! Our society could not survive such a radical practice of redistribution. I agree. Such practices are neither economically feasible nor sustainable, but I believe nonetheless that the prescriptions given to ancient Israel can teach us something valuable. The Israelite community was intended to be one characterized by radical justice. And Jesus, who Christians in the first-century saw as the embodiment of Israel and the fulfillment of Israelite law, came to proclaim justice, to preach to the poor, and to heal the sick. In essence, Jesus came to play God. He came to be God to humanity. Thus, the issue of justice is deeply related to medical ethics because it is deeply related to our lives on this planet as God intended them. We live in a radically unjust world, and it will take not only charity but also radical creativity on the part of the next generation of health care professionals to help us think through solutions to the problems of systemic injustice. Your task as pharmacists and people of faith is to reframe the ethics conversation in our time so that we can see playing God as more than wielding technology, for good or ill. As people of faith, we should come to see our purpose as health professionals in the larger context of God's purposes for justice and equity in a global community.

## Conclusion

In 1992, while my parents were living in Bogota, Columbia, I had the opportunity to visit that city and to meet Dr. Manuel Elkin Patarroyo at his lab at Hospital San Juan de Dios. Dr. Patarroyo is a pathologist who developed the world's first synthetic vaccine for malaria. Unfortunately, clinical trials of the vaccine yielded mixed results, and as he was working to improve the vaccine, the hospital where I visited him was closed due to lack of government funding. I will always remember one part of my conversation with the doctor. I asked him if any pharmaceutical companies had taken an interest in the vaccine. He told me that several had, and that one in particular had offered to buy the patent from him. I asked for how much. He smiled but never answered. "I turned them down," he said, "because I was afraid that the cost of the medication would have been too high for most in the developing world to pay." I learned years later that Dr. Patarroyo donated the patent to the World Health Organization in the hopes of providing an inexpensive and accessible cure for malaria to developing countries. In that moment he was playing God, and he continues to play God as he works on improving the vaccine to this day.

Many students I teach will someday join the world's elite wage earners. I hope to challenge them to use their skills, creativity, and intelligence to do justice, and in so doing, to play God.

## References


1. For three recent discussions of playing God as it applies to genetics, medical care, and reproductive technology, see Ted Peters, *Playing God?: Genetic Determinism and Human Freedom*, New York: Routledge, 2003; Jeff Lyon, *Playing God in the Nursery*, New York: W. W. Norton, 1985; and Mark O'Keefe, "Gender Choice: Is It Playing God?" in *Christian Century* 121, No. 9, May 4, 2004.
2. Quotation found online at http://www.imdb.com/title/tt0107497/quotes.
3. Michelle Roberts, "Scientists Make Eye's Retina from Stem Cells," BBC News, April 6, 2011. Found online at http://www.bbc.co.uk/news/health-12963297.
4. Ibid.
5. Data found online at http://data.worldbank.org/data-catalog/world-development-indicators/wdi-2010.
6. On a related note, both privileged and under-privileged populations face the temptation to view technology erroneously as the solution to every problem, or idolatrously as the substitute for an absent God (i.e. to play God as if God does not exist).
7. See Exodus 21:24, Leviticus 24:20, Deuteronomy 19:21, and Matthew 5:38-39.


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# Book Reviews

## Personal Identity and Fractured Selves: Perspectives from Philosophy, Ethics, and Neuroscience

Debra J. H. Matthews, Hilary Bok, and Peter V. Rabins, eds. Baltimore: Johns Hopkins University Press, 2009.

ISBN-10: 0-8018-9338-0; 203 PAGES, CLOTH, $57.00

"What has philosophy to do with medical care?" This imperfect analog of Tertullian's famous question, "What has Athens to do with Jerusalem?" is the overarching concern raised by the book *Personal Identity and Fractured Selves*, an interdisciplinary dialog between philosophical conceptualizations and the clinical approaches to personal identity in the context of neurologic brokenness. What constitutes personal identity? Is an individual with severe neurological dysfunction the "same person" as the one preceding the disorder, or are the disparities so significant that they qualify as "different persons?" The authorial anticipation was that both disciplines would be enriched through such dialog, expressing the hope that, through dialog, philosophical ideas would facilitate more philosophically rigorous neuroscientific research into personal identity (193). Unfortunately, the final conclusions demonstrated little reciprocity.

The book opens with preliminaries: a helpful review of various philosophical concepts within the semantic domain of personal identity, an exploration of the differing approaches and distinctive definitions of each of the invited contributors to these terms, and separate portrayals of the philosophical foundations and of the neurobiological understanding of personal identity. Following this, four case studies involving severe neurological disorders are presented which serve to ground the philosophical discussions and clarify the application of these concepts in clinical practice (187). The response to these case studies by three philosophers and two neuroscientists underscores not only the differences between the disciplines in their approach to personal identity, but also the intriguing distinctions within them.

These essays clearly evidence the highly disparate yet revealing presuppositional foundations, "languages," and, hence, thought processes that philosophers, neuroscientists, and clinicians bring to the issue of personal identity (x). For philosophers, personhood is purely theoretical, grounded in a Lockean understanding based on reason and experience, with a disregard for embodiment. Conversely, while neurobiologists focus on the physical mechanisms, personhood for clinicians is concrete and practical, grounded in a Darwinian-Freudian approach that employs innate biological variations along with irrational, unconscious mechanisms in personality development (166). Clinicians are not concerned about whether the neurologically "broken" individual before them is a person – or even the same person – but are concerned with how to care for them despite the philosophical ambiguity of their state of existence. Hence, the disparity lies in whether neurological dysfunction is envisioned as an ontic distinction or as a functional one (169).

Despite the intriguing novelty of philosophical musings about personal identity, humans are "much less rational, conscious, consistent and much more susceptible to self-deception in their self-construction" than philosophical theories allow (171). Frthermore, the failure of philosophers to holistically address the biological and social aspects of personal identity renders their theories less than adequate for application to the broken "flesh and blood" individuals and their fractured relationships with which clinicians are confronted. Individuals presenting for care are not "non-persons" or "different persons" but diminished and disordered selves (173).

The book is commendable despite the fact that, in the end, the disciplines talk past one another leaving little hope for agreement – much less consensus. It illuminates the variety of perspectives underpinning the cultural controversies surrounding personhood and personal identity. Many of our relevant laws are grounded in Lockean-based philosophical concepts, while physicalist understandings that undergird neurobiological research and Darwinian-Freudian concepts provide the basis for clinical science. Yet,

an understanding of the diverse philosophical concepts of personal identity and of research into the neurobiological functions of selfhood, while not determinative, will foster the wisdom of the clinician in the nurture of the broken individual who presents for care.

**Reviewed by Susan M. Haack, MD, MA (Bioethics), FACOG**, a consultative gynecologist at Hess Memorial Hospital and Mile Bluff Medical Center in Mauston, Wisconsin, USA.

## Progress in Bioethics: Science, Policy and Politics

Jonathan D. Moreno and Sam Berger, eds. Cambridge, Mass.: MIT Press, 2009.

ISBN-10: 0262134888; 308 PAGES, CLOTH, $19.00

"*The fatal metaphor of progress, which means leaving things behind us, has utterly obscured the real idea of growth, which means leaving things inside us.*"

– G.K. Chesterton, *Fancies Versus Fads*

"What is progressive bioethics?" wonder the editors of *Progress in Bioethics* (xvii). This is a great question, which fifteen contributors address through reflections on the nature of progressive politics and values, advancing biotechnology, the role of religion and other "value-laden" ideologies, justice in health care and medicine, and how bioethics should operate in public. Political science was, for Aristotle and other ancients, considered the surest path toward human flourishing for communities of individuals. *Progress in Bioethics* exemplifies a few ways that we have wandered from the ideal of seeking a thick moral account of how to share *eudaimonia* in public life. As with any edited volume, the whole does not necessarily represent the parts, but I offer three general worries that reveal what I suggest is, at bottom, a lack of philosophical precision and political virtue.

**The Autonomy of Science**

Many writers note progressives' concern for "getting the science" right, which is of course a legitimate concern. All bioethicists find themselves betwixt advancing scientific technique and ethical regulation – a sparkling few are even experts in both fields. By definition, science and ethics concern different spheres: science is concerned with physical reality and ethics is concerned with moral reality. Varying interpretations of this fact lead to vastly different bioethical principles. The reigning interpretation among conservatives and progressives alike is one of *conflict*: that scientific advance and ethical guidance find common ground only on a battlefield. Moreover, both progressives and conservatives are nobly concerned with finding a way to reconcile this conflict. The bioethical left emphasizes the autonomy of science, which allows for widespread, free, and mostly unbounded technological exploration.

I suggest an alternative to the violence metaphor: metaphysics as mediator, an overarching appreciation of the nature of technology, morality, *and especially* human beings (we, the technical–moral souls-incarnate) who are involved. No political agenda. No ideological tyranny over science. Ethics is concerned with the character and actions of moral agents. And by our nature, we are moral agents who practice science. Naturally, bioethical evaluation (and regulation, if we are to take the action-guiding nature of ethics seriously) will be deeply concerned with the metaphysics of morality.

**Eschewing Ideology**

In praise, a few essays offered outlying, insightful contributions on issues of ideology and values. William F. May's suggestion of a "campus" or "open terrain" for bioethics would provide for rich public discourse. Laurie Zoloth makes a religious appeal to challenge the scope of contemporary bioethics – suggesting greater attention on the poor, and ill and under-represented. Daniel Callahan's challenging discussion of medical advance and universal access to health care offers a welcome and stirring call to the good in public health and medicine.

But these pieces are a deviation from the book's norm of suspicion and distaste for moral and religious values. This is predicated on a dualism not unrelated to the science–ethics conflict discussed above. R. Alta Charo characterizes progressivism in bioethics as the Enlightenment value of dualisms: "logic versus faith… optimism versus pessimism… embracing vs. resisting" (52). James J. Hughes joins her to parade "the supremacy of reason over dogma and tradition" (163). Sociologist John H. Evans describes the public–private split that exists as the secular progressive standard, which soaks the leaves of *Progress in Bioethics*. Moreno and Berger reveal the ideological crisis within progressive bioethical identity: "Progressive bioethics must remain non-ideological…[y]et this lack of ideology should be restricted to means" (17). But this endeavor is headed for failure. The ethicist working without mention or use of ideology, value, or any sort of content-laden outlook (in the ends *and the means*) is essentially not doing ethics anymore. They might be doing science, which is inherently empirical; or politics, which likes to pretend about moral neutrality. But the fear and avoidance of ideology that enjoys the majority position

in *Progress in Bioethics* is simply not ethicizing. Of course, these contributors *are* doing bioethics, and so such an ideological crusade against ideology appears to be self-defeating.

**Playing Politics**

Despite their scientism and penchant for moral neutrality, the contributors make no effort to hide their political ideals: individual autonomy and choice, social justice and equality, technological optimism, pragmatism, pluralism, change, change, and, oh yeah, more change. But Marcy Darnovsky articulates a serious problem: "We have suffered through years of politically polarized environment that makes thoughtful deliberation about human biotechnologies difficult" (212). Lempert's shameless call for political tactics debases the bioethical enterprise, and Charo's take on bioethics as necessarily and hopelessly political (53) conflates the political with the public, which leaves us to the perils of the existing bipartisan political machine rather than reasonable, faithful, and neighborly public discourse.[1] Arthur Caplan's comment is a fair representation, I think: "[B]ioethics has taken a turn down a road [to politics] from which there is no return…bioethics has made a [political] bed it now must sleep in" (223). This acceptance of the entrenched status quo is inconsistent with the progressive political rhetoric we're all familiar with, which is constantly espoused in the book. And this suggests there is some change—some real, hopeful, growth for the human community – that progressives are unwilling to make.

*Progress in Bioethics* betrays a deep-seated insecurity about contemporary bioethics. Some contributors are anxious about bio-conservatism, which has had, these authors admit, notable influence over the past several years, punctuated by the leadership of the President's Council on Bioethics (2001–2009). Leon Kass bears the brunt of this anxious criticism: ten of the fifteen contributors quote and/or interact with Kass, most in attempt to discredit or ridicule his views.[2] An entire chapter is dedicated to "the New Conservative Crusade," and the general tone (with a couple of exceptions) is flooded with a hyper-awareness of conservative moral and religious ideology. This strategy is at best rhetorically and philosophically dissatisfying; at worst, it deflates (even undercuts) the book's attempt to construct a coherent and clear identity for progressive bioethics. The tired jargon just plays badly. But this appears to be the fatefully bipartisan and ethically *thin* political endeavor most of us expect – each side existing as a reaction to the other.

**Endnotes**

1. For an inspiring suggestion to "decouple the political and the public," see James Davison Hunter's *To Change the World* (Oxford: Oxford University Press, 2010).

2. For a much different perspective on the Kass Council, see Adam Briggle's *A Rich Bioethics: Public Policy,*

*3. Biotechnology, and the Kass Council* (Notre Dame, IN: University of Notre Dame Press, 2010).

**Reviewed by Evan C. Rosa (BA Philosophy),** Communications Director of the Center for Bioethics and Culture and is a Fellow of the Paul Ramsey Institute; he is pursuing an MA in philosophy of religion and ethics at Biola University, La Mirada, CA, USA.

## The Ethics of Organ Transplantation

Stephen J. Jensen, Editor. Washington, D.C.: The Catholic University Press of America, 2011.

ISBN: 978-0813218748; 339 PAGES, PAPER, $24.95.

## The Ethics of Transplants: Why Careless Thought Costs Lives.

Janet Richards. Oxford and New York: Oxford University Press, 2012.

ISBN: 978-0199575558, 256 PAGES, CLOTH, $29.95

In spite of the significant medical advances we have made within the area of organ transplants in the past 60 years, the unalterable fact remains that we do not have a sufficient number of organs for the number of persons needing them. The significant advances that we have also made that enable medical practitioners to keep alive those who, during this time, would ordinarily have died raises additional questions about when life ends, when death occurs, and what is permissible during that sometimes blurry line in between. A number of important issues exist within the practice of organ donation, with often contrasting answers. Both of these volumes attempt to address some of these concerns, the first from a largely traditional Catholic perspective, and the other from the perspective of a moral philosopher working in the area of practical ethics.

*The Ethics of Organ Transplantation*, an edited and interdisciplinary volume, arose out of a 2009 conference held at the University of St. Thomas in Houston, TX. The contributors include theologians, philosophers, and physicians, and the book is divided into five major sections: Brain Death (challenges brain death as a legitimate criterion of death), Donation after Cardiac Death (exploring the issue of non-heart-beating organ donation), The Dead Donor Rule (prohibits taking vital organs from a living person), Gift or Conscription (to what extent is organ donation voluntary), and Corollaries and History (with one article comparing how the Church argues with regard to gestational surrogacy and organ donation, and the other asking the question to what extent can non-definitive Church teaching be challenged by theologians). Utilizing church history, arguments of numerous theologians, as well as important church documents, the articles generally support the Catholic Church's teaching regarding prohibition of live donation of vital organs (including by those in a brain dead state), the emphasis on the dignity of all human beings, and possible abuses with regard to obtaining organs for both the donor and the recipient. Two essays stand out in terms of the different subject matter and approach they take. Thomas I. Cochrane, in "The Dead Donor Rule," makes the bold assertion that the person who is dying and wishes to forgo life-sustaining therapy in order to donate their organs should be permitted to do so, and that the physician removing the organs is not causing that person's death. David Matas, in "Ethics of Contact with China on Transplants," provides evidence of the practice of the Chinese government to obtain most of their organs for transplant from prisoners slated for execution, as well as for practitioners of Falun Gong. All of the articles are extremely well researched, quite scholarly, and each presents clearly articulated arguments for its position. Those whose views align with the Catholic Church will particularly appreciate this volume.

*The Ethics of Transplants* is a single-author work that is quite theoretical, focusing particularly on critical analysis of the ethics of organ transplants, while utilizing organ procurement as a way to illustrate careful moral reasoning. Thus, the scope is admittedly narrowed, and does not attempt to deal in a comprehensive manner with all of the possible issues related to organ transplants. Richards does not simply focus on the pro and con arguments, but rather addresses the deeper issues behind the arguments, in particular the presumptions, premises, and conclusions. The book presumes that organ transplantation is important, and that we need more organs. The question of how to do this is what is debatable. The book considers both the issue of procurement of donors from the living as well as from the dead. The former she addresses in the second chapter, and provides a clear window into her purpose in writing the volume. She asks the question about whether it is permissible for people to sell their own organs, as long as it does not cause their death (e.g., kidney or cornea donation). She maintains that most would argue "no," and would use a form of argumentation, which she calls "one-liners" – arguments based on general moral principles. She challenges these arguments one by one – that it is coercion due to poverty,

is exploitation of the poor, is an affront to human dignity, results in the commodification of the human body, and that disallowing it would result in the persistence of black markets, as well as other arguments – and systematically deconstructs them utilizing analogies and thought experiments. While one may not necessarily agree with her conclusions, her book demonstrates the way one can go about exploring deeply what at times could be the uncritical acceptance of general principles. Because of its scholarly and strong philosophic underpinnings, this book would be of most interest to moral philosophers working in the field of bioethics, or even those working in the area of practical ethics, in which this book could function in a classroom setting, as an example of how to critically analyze a moral argument.

Organ donation and transplantation continues to be an important and controversial issue in health care ethics. With the continued shortage of organ donors and, subsequently, organs, hard questions need to addressed about how best to ethically procure more organs, how best to minimize harm both to donors and recipients but especially the former, how to define death, and how to determine and protect consent. Both volumes do a good job of continuing the discussion of critical thinking, and with their different approaches and answers, demonstrate just how difficult moral reasoning can be.

**Reviewed by Donna Yarri, PhD (Religious Studies),** who is an Associate Professor of Theology at Alvernia University in Reading, Pennsylvania, USA.

## The Soul of Medicine: Spiritual Perspectives and Clinical Practice.

John R. Peteet, MD and Michael N. D'Ambra, MD, eds. Baltimore: Johns Hopkins University Press, 2011.

ISBN 978-421402994; 260 PAGES, CLOTH, $50.00

It is increasingly recognized that something vital is missing from the contemporary paradigm of bio-psycho-social medicine; that something is the soul. The soul, broadly conceived, and its expression in the context of health and healing is the subject of *The Soul of Medicine: Spiritual Perspectives and Clinical Practice*, edited by John R Peteet, MD, and Michael N. D'Ambra, MD. Through a series of essays, the editors illustrate the integral complexity of the spiritual nature of the persons who present for medical care and of the professionals who care for them.

After a historical overview of the relationship of spirituality and medicine, followed by a "philosophical" argument for the importance of spirituality in health and healing and the need for integration of spirituality in the care of patients, the book devotes the next nine chapters to the intersection of individual faith traditions (Judaism, Hinduism, Islam, Christianity, Buddhism, Eclectic Spirituality, Christian Science, Jehovah's Witnesses, and a secular perspective) with medical care and practice. These chapters, all written by "practitioners," follow a prescribed pattern with individual modifications. Each begins with the basics of the particular faith tradition, addressing its ultimate nature, its essential concerns, and its insights into life and healing. This is followed by a discussion of the relationship of the faith tradition to contemporary medical practice, exploring how beliefs of the practitioner influence the practice of medicine, how the spirituality of the patient is accessed in practice, and the challenges and reinforcements of the tradition to contemporary medical practice. The book concludes with chapters on the implications of spirituality for the profession of medicine, a discussion of the importance of integrating chaplaincy into the care team, and the challenges of incorporating these principles and ideas into contemporary training programs.

In its approach to spirituality, *The Soul of Medicine* is not prescriptive, but descriptive: it does not prescribe methods for the spiritual care of patients, but rather describes a diversity of spiritual realities encountered in medical care. It gives voice to the variety of faith (and non-faith) traditions met in the course of patient care and the need for awareness and sensitivity to these spiritual aspects which powerfully impact one's understanding of illness and healing, living and dying.

The book's approach is liberal, but perhaps not inappropriately so, given that the intended audience includes both medical practitioners and students in pluralistic, secular institutions. Concepts are defined openly and broadly to encompass the full range of possibilities. In that light, the term "spiritual," defined as a person's "connection to a larger or transcendent reality that gives meaning to life," is preferred to the term "religious" which portends a particularist community (x); and the definition of health employed is that of the World Health Organization: "a state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity" (28). Yet, curiously, the preferred term for medicine in this book is "biomedicine," chosen to distinguish it from other healing traditions. This term, which appears as the very first word in the preface of the book, is later narrowly defined as "an approach to health and healing" that is characterized by materialism, reductionism, empiricism, and objectivity (9), a definition that further illuminates the particular perspective of the authors.

Despite the overall value of the book, the premise and argument of the first chapter, entitled "Spirituality and Biomedicine: a history of harmony and discord" was unconvincing. In this chapter the authors attempt to bifurcate the nuanced history of spirituality and medicine, categorizing that history into "either/or" boxes of "harmony" and "discord," an impossibility in our complex world. The ultimate division was drawn between "physician-cleric" and "physician-scientist," a contrived distinction that is rarely applicable in life or practice. From their vantage point, the original impetus for the discord between spirituality and medicine was attributed to the Fourth Lateran Council of the 13th century, a fact and a date that are loosely cited and of questionable significance. Ironically, here the term "religion" is used rather than "spirituality," citing it as a causative factor in the discord. Furthermore, although specifying that this was not an exhaustive overview, the important role of early Christianity in medicine and health care (other than the work of Basil of Caesarea) was largely ignored (see Gary B. Ferngren, *Medicine and Health Care in Early Christianity*).

It would be difficult to read this book without being humbled—humbled by the similarities and yet profound differences of our various spiritual and faith traditions—humbled by the task of our calling as medical professionals to address the many spiritual perspectives we encounter in daily practice. It is in this light that the book emphasizes the need for chaplaincy as a separate specialty on the care team – specific chaplains to care for persons of specific faith traditions. Embedded in the idea of professionalism is also a call to professionals to know and understand their own spirituality, so that they can better attend to that of their patients.

This book provides a fascinating, enlightening, and at times overwhelming overview of the plurality of spiritual voices encountered in the practice of medicine. Moreover, it highlights the sobering reality of the complexity of integrating spirituality into the practice of medicine in a pluralistic culture. *The Soul of Medicine* is therefore a valuable read for anyone involved in the care of patients, especially those who are located in urban centers where there exists a plurality of ethnicities and faith traditions that one is likely to encounter.

**Reviewed by Susan M. Haack, MD, MA, MDiv, FACOG,** a consultative gynecologist at Mile Bluff Medical Center, Mauston, WI, USA.

## Chimera's Children: Ethical, Philosophical and Religious Perspectives on Non-Human Experimentation

Calum MacKellar and David Albert Jones, eds. London and New York: Continuum, 2012.

ISBN: 978-1441198860; 208 PAGES. PAPER, £18.99

Divided into three parts, this book begins with a look back at ancient myths about half-human and half-animal creatures, more recent science fiction, as well as present-day national and international legislation. It then moves on to cover developments in the creation of human-nonhuman combinations, showing that the reality of modern science has overtaken science fiction in its efforts to produce mixed-species organisms. The third and final part discusses different cultural and religious perspectives and provides philosophical reflection on the ethics of the new technologies which allow us to transfer not only single genes from one species to another but even to create human-nonhuman embryos by transferring the nucleus of a human cell into the egg of, say, a rabbit.

Starting with definitions of technical terms used to refer to various types of inter-species organisms, the chapter on national and international legislation offers a comprehensive overview of laws and regulations worldwide, noting that most countries lack adequate guidelines regulating the creation of interspecies entities. While most countries that have legislated in this area have placed limits on human-nonhuman combinations, the United Kingdom expressly facilitates the creation of such entities. In addition, in the United States of America almost all forms of research are legally permissible if privately funded and not intended to produce a commercial product; Japan also has permissive legislation, whereas Canadian and Australian legislations are prohibitive,

The second part discusses and evaluates scientific developments, past, present and future, Various procedures resulting in organisms with genes or chromosomes from more than one species are detailed and explained in terms that are intelligible to the non-scientific layperson. The legal frameworks for the procedures are revisited with a view to highlighting public and national attitudes to this kind of science. The volume expresses scepticism about the usefulness - for any purpose - of the creation of human-nonhuman cytoplasmic hybrid embryos, that is, embryonic organisms created by inserting the cell nucleus from a human somatic cell into an enucleated animal oocyte. For example, their use in human embryonic stem-cell research is questioned due to the potential incompatibility of animal mitochondria and a human cell nucleus. The author states, "Cytoplasmic hybrids, right from the beginning and throughout later developmental stages, may be unnaturally dysfunctional." (98)

Noting that we live in a global environment that is multicultural, it is argued that governments and ethics bodies have a duty to seriously consider the ethical, religious, and political views of their populations when introducing legislation that raises questions about human nature and human dignity – indeed, about what it means to be human. Thus, the third part of the book presents a brief overview of how the major religions see the relationship between humans and animals. At the conclusion of part three, the author addresses ethical issues from a philosophical perspective, discussing a range of concerns including medical and psychological risks, human and animal rights, environmental implications and the spectre of eugenics. Also raised are questions about personhood and personal identity as well as about the importance of human gametes and genes.

This book is a valuable source of information for the scientist, ethicist, or politician, as well as for the layperson wanting a guide through the legal and moral maze in the field of human-nonhuman interspecies experimentation. Moreover, the science involved is explained in simple terms for those who know little but want to know more about what is going on in this area of research.

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

## Consciousness: Confessions of a Romantic Reductionist

Christof Koch. Cambridge, Mass.: MIT Press, 2012.

ISBN: 978-0262017497; 181 PAGES, CLOTH, $24.95

The great scientific strides made by early Enlightenment scholars have often been attributed to the Judeo-Christian worldview of those scholars – belief in a God who created an ordered world that could be known and tested by human reason. Unfortunately, reason quickly came to reign over that worldview, which shift relegated God to the gaps in human knowledge and eliminated God from epistemic explanations and scientific writings. That is, until the publication of *Consciousness: Confessions of a Romantic Reductionist* by Christof Koch, a hauntingly eccentric book addressing the neurobiology of consciousness. Koch addresses a highly complex subject in an easy, conversational, and narrative style that engages the reader even when the material is not entirely comprehensible. It is much more than just another book on the neurobiology of consciousness: it is a peculiar combination of Koch's scientific, personal, and spiritual journeys – a combination of apology, confession, testimony, and proclamation of "good news." It is permeated with a rich heritage of religious, scriptural, and theological language – yet looks are deceiving. Unlike early enlightenment thinkers whose search for meaning and significance through scientific understanding confirmed their faith in God, Koch's journey through neurobiological research takes him in the opposite direction, away from God, despite the paradoxical richness of his religious language.

Koch begins his book with history: a history of the "mind-body" problem, the history behind his search for meaning, his desire to demonstrate the inadequacy of science for understanding the nature of the mind-body divide, and a history of his Catholic upbringing.

Enter: Frances Crick, his mentor. Exit: faith in a personal God.

His scientific journey is written in an apologetic style, highlighting a series of laboratory and clinical experiments that demonstrate the association between conscious phenomena, unconscious neural activity, and neural functions – an apology for his faith in science and reason. His underlying presupposition is that there can be no cause and effect between the immaterial and the material. He willingly detours into the "Valley of Free Will," demonstrating that there is no neural correlate to the classical notion of free will, only a phenomenal feeling of agency for which he cannot account. Journeying then into information theory, he finally discovers the bud of consciousness in the womb of integrated information theories – what he terms panpsychism: the entire cosmos, including every single living cell, is sentient (inconsistent with his belief that denies sentience to PVS patients, from whom, he claims, consciousness has fled). His conclusion: there is no soul; integrated information gives rise to conscious sensation or thought.

Koch is a fascinating man – a philosopher and scientist, well versed in literature, a renaissance man of sorts. But more than a scientific argument, Koch's book is a personal testimony of his rejection of the Christian faith and the acquisition of a newfound faith in empirical science and rationality. Koch is the epitome of the reductive physicalist lamented by Harold Langsam in his book, *The Wonder of Consciousness.* Unlike Langsam, though, Koch demonstrates no true sense of wonder – only the zeal to discover, to know, to gain notoriety, and to gain power over consciousness. In true postmodern fashion, Koch preserves the language of his original faith tradition but transfers the meaningfully rich religious terminology onto objects of his new scientific faith, thereby retaining the form but altering the substance – a practice that is deceptively disorienting. Moreover, there is an ironic inconsistency in his reductionist worldview; with Peter Singer, he sings the "anti-speciesism song" that mankind is no different from other animals and deserves no special place in the creaturely order based on consciousness. Yet, he justifies animal experimentation on the basis of the amelioration of human suffering, offering no rationalization for why human suffering matters more than that of animals.

From the beginning, his retention of religious language fosters a hope that, despite the negative influence of Crick, Koch will return to his roots. However, the final chapter presents a sad, conflicted picture: having rejected his belief in a personal God, Koch has found neither the Holy Grail (the neural correlates of consciousness) nor meaning in the universe. Furthermore, any residual meaning has been challenged by the loss of an infant daughter to SIDS, then the serial losses of his father, his adult children from the

home, his mentor Frances Crick, and his beloved dog. In response to all of this, he leaves his wife of 30 years, all part of the "confession" promised in the subtitle. Ultimately, after losing or being estranged from everyone meaningful in this life, he relates his attempt to run to the top of a mountain after drinking a bottle of wine. Coming to his senses, though, he turned back and shouted, "I am the master of my fate. I am the captain of my soul." Paradoxically, he claims to be saddened by the loss of his religious beliefs, "an inevitable part of growing up," yet he ends his book with a psalm from the Dead Sea Scrolls which speaks of "hope" for creatures molded out of dust to have consort one day with things eternal.

*Consciousness* is a hauntingly engaging book for both its scientific insight and personal tragedy. But for what audience was this book intended? It is doubtful that it was intended for the scientific community or for the religious community – for neurobiology students, perhaps. One cannot escape, however, the intuitive sense that the book was written for the sake of the author alone, serving as a purgative and self-justificatory act in an attempt to discover meaning in his life and world, a meaning lost by the rejection of his faith. Or, perhaps it is meant as a warning to any who may choose to venture down this same reductionist path.

**Reviewed by Susan M. Haack, MD, MA, MDiv, FACOG,** a consultative gynecologist at Mile Bluff Medical Center, Mauston, WI, USA.

## The Biology of Sin: Grace, Hope, and Healing for Those Who Feel Trapped

Matthew S. Stanford. Colorado Springs and Secunderabad, India: Biblica, 2010.

ISBN: 978-0830856138, 166 PAGES, PAPER, $18.00

This is a brief and straightforward book that, within the context of what the author understands as the biblical teaching about sin and grace, does two things. Firstly, it informs us about various forms of sin from a neuroscientific perspective. Secondly, it relates a number of stories about healing. Rage, lust and adultery, lying and stealing, addiction and homosexuality are all treated. An appendix lists the counseling and ministry resources available in the United States.

There are two good things about this book. The first is the scientific description by someone eminently qualified to give it. The second is the author's record and celebration of the grace of God. Only a narrow-minded reader will question the significance of a physiological, along with a spiritual, account of sin; only a hard-hearted reader will not be saddened by the account of human brokenness. If this book impresses on us these things, along with the supreme assurance of the power of the gospel of Christ, it will have achieved an important goal.

However, the book also reveals the crying need for Christian scientists delving into these questions not to go it alone, but rather to work in conjunction with theologians and moral philosophers. Theological claims made in this book are sometimes controversial and sometimes simply mistaken. Matthew Stanford claims that "there is no difference in the 'seriousness' of sins in God's eyes; to him, sin is sin" (9). Late at night, a patient and godly person is briefly and uncharacteristically irritable on account of tiredness. On Stanford's logic, this is just as serious as the late-night plotting on his computer of a serial pedophile. I cannot believe that Stanford really believes that, but it is what he says. We also read that "[h]uman anger, while originally created in the image of God's anger, has been tainted by sin" (40). But no anger marks the eternal triune relationship of Father, Son and Spirit, in whose image humans are created. Theologically, this volume is seriously flawed (and I refrain from comment on the merely controversial).

Further, Stanford does not even raise, let alone answer, the question of how physiological or social facts bear on moral responsibility. If, for example, a particular individual's propensity to anger or sexual orientation is partly explicable in terms of physiological distinctives, does that not diminish or affect moral responsibility? The author's answer is: "Certainly not," but he does not tell us why not. Neuroscientific data, theological statements and personal stories are thus juxtaposed, but they are not connected in any kind of coherent account. If the physiological and socio-environmental facts are as they are often portrayed to be, a lot of moral reasoning is required to explain how responsibility for sin is to be understood in relation to them. I am not implying that such facts do away with responsibility, only that we need to know how it all adds up. The author can scarcely be unaware of the issue; yet he writes as though he were. The lesson to be learned, then, is that inter-disciplinary collaboration is needed. This is a matter of first importance.

**Reviewed by Stephen N. Williams, PhD**, who teaches philosophy at Union Theological College in Belfast, Ireland, UK.

## Justice Between the Young and the Old

Dennis McKerlie. New York: Oxford University Press, 2012.

ISBN: 978-0199769131; 240 PAGES, CLOTH, $65.00

Most governmental social programs designed to comfort and sustain a nation's populace in their old age were not designed to account for ever-increasing life spans. As the United States and other nations contemplate these financial obligations, a return to the philosophical reasons of why the young and middle aged can or should be called upon to aid and support the old is necessary and important. Dennis McKerlie has been dealing with the complexities of justice and age through much of his academic career and offers a dense and thorough work of moral philosophy in *Justice Between the Young and the Old*. McKerlie not only articulates his own vision of the obligations of justice with regards to age, he clearly demonstrates how and why his perspective is different from other writers in this field.

The primary point of departure is McKerlie's view that justice is best applied at temporal life stages as opposed to full life spans. This shift necessitates a movement away from equality being the central egalitarian principle used to assess justice between age groups. Instead, priority is to be the most important principle applied, as it is more functional when dealing with well-being at a given life stage. McKerlie also cautions that priority is based upon current need and should not lead to utilitarianism. The goal of justice should be to ensure that each individual has a sufficient level of well-being at a given life stage as opposed to maximizing their utility over a completed life or maximizing the well-being of the community in total. When the individual is making choices for themselves in their youth or middle age that may impact their well-being in old age, McKerlie recommends prudence. Again, prudence must be applied in a manner that does not slide into utilitarianism or hedonism. Sometimes individuals may have to choose less of a good in the present so that it can be distributed across life stages or be of benefit when conditions are worse. McKerlie also addresses changing values in the course of an individual's life, including a chapter specifically addressing the changes in values and autonomy associated with Alzheimer's disease.

A very practical problem of determining justice between age groups is discussed at the conclusion of the book. Who qualifies as being old when the definition is based upon life expectancy as normative expectancy, which continues to change, and which is also culturally varied? While this reality is inherent in this field and does not weaken McKerlie's thesis in the slightest, it does make employing these theories difficult.

Application of McKerlie's work is left to the reader. While the author does briefly touch upon social security programs, there is scant mention of how these ideas should guide health care policy, allocation of medical resources, etc. This book is an excellent work of theoretical moral philosophy that both stands on its own and can be quite useful as a resource to those doing applied ethics or formulating policies in which distribution across ages is a significant concern.

**Reviewed by Corey R. Harris, PhD,** who is an Assistant Professor of Theology at Alvernia University in Reading, PA, USA.

## Hippocratic, Religious, and Secular Medical Ethics: The Points of Conflict

Robert M. Veatch. Washington D.C.: Georgetown University Press, 2012

ISBN: 978-1589019461; 242 PAGES, PAPER, $29.95

Developed out of the Gifford Lectures that he delivered in Edinburgh in 2008, Robert Veatch's book is an indictment directed against the Hippocratic Oath. With focus on medical ethics, and true to the tradition of the Gifford lectures, it explores the relationship between science, religion, and philosophy.

Seeing the Hippocratic Oath as sectarian, paternalistic, and reflective of a pagan religion, Veatch describes the oath as both controversial and offensive. In addition, he sees it as too patient-centred, arguing that medicine needs to also take into account the social interests of public health. Accusing the medical profession of acting as a secret society in the past, he says that it is not a prerogative of any professional group to lay down norms and impose them on lay people obtaining services from the profession.

Thus, the book starts with a critical overview of Hippocratic influences on ancient and medieval thought and on many of the codes of the last century. Highlighting what he sees as their main shortcoming, he says that norms of professional conduct must be based on ethical standards agreed on both by the professionals and the laypeople with whom they interact. This requirement rules out ethical norms that cannot be accepted by both secular and religious minds. Veatch, therefore, dismisses Roman Catholic medical ethics inasmuch as it is based on Scripture and tradition in addition to natural reason. He also dismisses the theocentric medical ethics of Karl Barth and Stanley Hauerwas, as well as that of Tristram Engelhardt after his conversion to Orthodoxy.

A medical code based on ethical standards agreed on by physicians and laypeople alike can, Veatch argues, only be achieved if medical codes are rooted in a general ethical system widely embraced by both secular and religious sectors of society and based on reason and experience. In the last part of the book, then, Veatch explores similarities between different attempts to spell out widely acceptable rules of medical ethics, including the four principle based medical ethics of Beauchamp and Childress, Baruch Brody's five appeals, and his own seven-principle theory, as well as others. What he finds is that there exists a basic and common morality or convergence of basic moral norms. Nowhere else is this as well exemplified, he argues, as in the Universal Declaration of Human Rights of 1948 and the Universal Declaration on Bioethics and Human Rights of 2005.

There is scant recognition in this book of the understanding that the very ends of medicine, to some significant extent, ought to direct medical practice and, thus, promote a certain ethos and ethics of care for the patient in need; that is, an ethos and ethics that remains largely patient-centred, while not neglecting the health interests of society at large.

Fiercely opposed to Hippocratic or religiously-based ethics, the book may be recommended to students and lecturers of different convictions as a provocative and challenging starting point for discussion about the foundations of medical ethics.

**Reviewed by Agneta Sutton PhD,** who lectures in Bioethics at Heythrop College, University of London in London, England, UK.

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