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Origins and Endings

Maternal-fetal conflict, heritable genome editing, and palliative sedation

Penn Bioethics Journal

The Penn Bioethics Journal (PBJ) is the premier peer-reviewed undergraduate bioethics journal. Established in 2004, the Journal provides a venue for undergraduates to make contributions to the field of bioethics.

Embracing the interdisciplinarity of bioethics, PBJ reviews and publishes original work addressing debates in medicine, technology, philosophy, public policy, law, theology, and ethics, among other disciplines. The biannual issue also features news briefs summarizing current issues and interviews with eminent figures in the field.

Authors and the editorial staff alike have a unique opportunity to experience the peer-review process through the collaborative, rigorous review and preparation of the Journal. With an audience ranging from undergraduates to scholars in the field to the broader public seeking unbiased information, the Penn Bioethics Journal occupies a unique niche in the field of bioethics.

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Content

Letter from the Editor

Dear Readers,

It is my pleasure to present you with Volume XV, Issue ii of the Penn Bioethics Journal entitled "Origins and Endings." The features in this issue investigate ethical decision making at the beginning and end of human life.

In our first article, "Who Forced the C-Section? Maternal-Fetal Conflict and Different Objectives of Care," Tarika Srinivasan of the University of Texas at Austin examines the differences in perspective between pediatricians and obstetricians on mandated C-sections and the ethics of seeking legal action against non-compliant mothers. She argues that forced C-sections violate maternal autonomy and undermines the physician-patient relationship.

The second paper in this issue, "Hubris or Helpful? Ethics and Governance in Heritable Genome Editing," examines the implications of applying germline genome editing to genetic correction and enhancement. Connor Tou from the University of California, Berkeley, contends that international consensus on the regulation of heritable genome editing is imperative.

Our third article is titled "Palliative Sedation: Masked Euthanasia or Compassionate Care for the Dying?" and explores the use of sedation to relieve pain in palliative care. Author Naomi DeTemple from Trinity International University asserts that responsibly administered palliative sedation can be an ethical approach to care for the dying that preserves patient dignity.

For this issue, we had the pleasure of interviewing Dr. Steven Ralston, a professor of Clinical Obstetrics and Gynecology at the Perelman School of Medicine, and Dr. Jennifer James, a neonatologist at the Children's Hospital of Philadelphia. Dr. Ralston and Dr. James share their expertise in maternal-fetal medicine and discuss physicians' responsibility in resolving conflict during pregnancy and delivery.

Our Bioethics-in-Brief section presents three news briefs covering current events in bioethics. The first brief explains the status and results of ongoing litigation against pharmaceutical companies and distributors for their role in the opioid epidemic. The second brief discusses the complexity of protecting the human right to health for migrants and refugees. The final news brief examines the public debate surrounding Canada's Medical Aid in Dying policies.

I would like to express my gratitude to the authors and interviewees who contributed to this issue. I also want to thank our faculty advisor, Harald Schmidt, for his support during the editing and publication processes. Finally, I am incredibly grateful for the staff of editors and their commitment to PBJ. It has been a privilege to work with and learn from with the dedicated members of the Journal, and I am looking forward to seeing how the next generation of editors further the growth of this organization. I hope the content in this issue inspires you to delve into bioethics and engage in dialogue about the current issues facing this field.

Emma Balaan
Editor-in-Chief
University of Pennsylvania C'20

Bioethics-in-Brief

Opioid Litigation Continues with Settlements and Uncertainty

Raksha Dondapati

Recently, several pharmaceutical companies have come under fire for their role in the opioid epidemic, and litigation against them is ongoing. A large federal case in Ohio with over 2,000 lawsuits has targeting manufacturers like Purdue Pharma as well as distributors like CVS and Walgreens. (Lopez 2019) The plaintiffs include cities, counties, tribal authorities, and individuals. (Dwyer 2019)

With regard to manufacturers, the cases argue that misleading marketing downplayed the risk of opioids and exaggerated their benefits. With regard to distributors, the cases argue that opioid drugs were supplied despite knowledge that they would be overused. Both manufacturers and distributors have denied the allegations. (Lopez 2019) They claim that opioid medications have been highly regulated by federal officials, and that for pills to be sold, physicians had to write prescriptions. (Dwyer 2019)

The most publicly followed case is one involving Purdue Pharma, the manufacturer of OxyContin. The company and its owners, the Sackler family, have reached a tentative settlement with 23 states and more than 2,000 cities and counties. The agreement stipulates that the company will declare bankruptcy and dissolve (the company has since filed for Chapter 11 bankruptcy); a new company, managed by a group of trustees, will be formed and will continue to sell OxyContin, with the sales revenue going to the plaintiffs in the settlement. Purdue Pharma will also donate drugs for addiction treatment and overdose. In total, the deal is said to be worth $10 to $12 billion, the largest payout yet. However, the settlement does not include a statement of wrongdoing. (Lopez 2019) Purdue Pharma's bankruptcy filing has frozen the lawsuits against them and shifted the claims to bankruptcy court. (Joseph 2019) A federal bankruptcy judge put all lawsuits against the company on hold until April so that the sides can continue to work on a settlement. This news came after the company agreed on an expanded list of conditions for delaying litigation, including a $200 million fund for organizations targeting the opioid crisis. (Mulvihill 2019) Purdue Pharma previously settled in Oklahoma for $270 million, and had a case in North Dakota thrown out. (Bernstein, Davis, et al. 2019)

Johnson and Johnson reached a $20.4 million settlement with two Ohio counties, $5.4 million of which will go to nonprofits for opioid-related programs. Mallinckrodt Pharmaceuticals, one of the largest generic manufacturers of opioids in the United States, announced a "settlement in principle" of $24 million in payments, as well as $6 million in medications (e.g. for addiction treatment). (Bernstein et al. 2019) Distributors AmerisourceBergen, Cardinal Health and McKesson and manufacturer Teva Pharmaceuticals reached settlements amounting to a total of $260 million. Endo International agreed to one worth $10 million, and Allergan has agreed to a "settlement in principle" reported to amount to $5 million. (Castele 2019) Again, these deals also do not include any admission of wrongdoing. (Mann and Dwyer 2019) Other companies have also reached settlements; notably, Walgreens is the only original defendant that has not reached a settlement. (Dwyer 2019) The companies that do not reach settlements will eventually go to trial.

In September, U.S. District Judge Dan Polster, who is overseeing the entire case, approved an expansion of the number of communities that could benefit from class action suit against drugmakers, meaning that tens of thousands of cities, counties and other local governments will be automatically included in future opioid-related settlements.

Several jurisdictions also have their own cases against companies as well. Many cities and countries want to pursue their own legal action against Purdue Pharma and the Sackler family, as well as other companies.

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Bioethics-in-Brief

Medical Aid in Dying in Canada Incites Controversy

Timothy Jiang

Since the introduction of Bill C-14 in 2016, Medical Aid in Dying (MAiD) has allowed over 7000 Canadians to willfully end their lives (Health Canada 2018). Statistically, this number comprises one percent of all Canadian deaths in the last three years. To receive Medical Aid in Dying, a patient must first experience what is stated as "intolerable suffering", and must write a written statement expressing their utmost desire to end their lives. To ensure that this is happening free of coercion, two independent witnesses must be present when this statement is being signed (Bill C-14, 2016, Preamble). As a further safeguard against unsuitable euthanasia, two separate physicians must also confirm that the patient is in "an advanced state of irreversible decline" and that the patient's "natural death is reasonably foreseeable" (Bill C-13, 2016, Eligibility).

Though these multitude of checkpoints are in place to deter impulsive or short-sighted requests of euthanasia, opponents of MAiD say that these checkpoints are not adequate in prevention and that they are often not executed properly by health care professionals. In late July 2019, Alan Nichols, a depressed yet otherwise healthy man, was assessed and approved for MAiD eligibility. Although he was not terminally ill, nor was he in "an advanced state of irreversible decline", physicians still gave the go-ahead to proceed with euthanasia, without consulting his family. His family argued that Nichols was not in a sufficiently stable mental state to make his decision, something they contend should disqualify individuals from MAiD eligibility (Symons 2019).

Shortly after this incident, in mid-September 2019, Superior Court Judge Christine Baudouin significantly loosened constraints for the approval of MAiD, fueling public debate over to an already contentious subject. Baudouin struck down the provision that required patients to be terminally ill for euthanasia consideration, stating that denying access to assisted dying "forces [patients] to endure harsh physical and psychological suffering" (Grant 2019). Euthanasia proponents celebrate this advancement, asserting that candidates who were originally denied MAiD under old provisions would resort to more inhumane and painful methods, such as starvation or self-inflicted wounds (Cook 2019). Opponents' sentiments are summarized well in Dr. Michel Racicot's view: "If we remove this criterion, we do not transform medical aid in dying into help for the dying person. Instead, medical aid in dying becomes death on demand for people who are suffering, but who may still have a long life ahead of them" (Cook 2019).

There are many issues to consider when weighing the ethicality of various implementations of MAiD. First and foremost, when dealing with any level of physician-prescribed euthanasia, the bioethical principle of benefience may be at stake. The principle of beneficence states that any medical procedure must be enacted with the intent of doing good for the patient, and what is considered "good" is largely up to interpretation. Physically, the act of euthanasia is unequivocally deleterious to the patient; however, one may argue that ending the patient's suffering is of even greater importance. This then calls into question another core bioethical tenet, the principle of non-maleficence, which holds that procedures should strive to minimize harm. If citizens deem that ending a patient's mental suffering at the cost of his or her life achieves a net positive impact for society, then Judge Baudouin's loosened constraints on euthanasia elligibility are ethically justifiable.

Ultimately, a majority of citizens believe that euthanasia is permissible when a patient experiences excessive, incurable physical pain. However, this heated debate boils down to determining the threshold a patient's suffering must surpass to justify euthanasia.

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Humanitarian Justice: Rethinking Bioethics, Human Rights, and Health

Jordan Liu

In an era known for political divisiveness and closed borders, humanitarianism has emerged as a formidable voice in the global moral conversation. Humanitarian actors have become dominant forces in the fight for social change, and NGOs like Médecins San Frontières (Doctors Without Borders) are now synonymous with altruism, selflessness, and even martyrdom.

Yet, times are changing. Throughout the world, the political tide is shifting towards nationalism and isolationism, and once-glorified humanitarian ideals are facing challenges unlike any before.

In the Mediterranean Sea, millions of refugees fleeing war and instability have embarked on the dangerous route to European shores, where they seek freedom, opportunity, and peace. In the process, tens of thousands have drowned, transforming the idyllic sea into "the world's deadliest migration route" (Human Rights Watch 2019). Sea-Watch, a humanitarian NGO, is among the stakeholders devoted to addressing the crisis by rescuing drowning migrants and providing free emergency medical care.

Since its founding in 2015, Sea-Watch estimates that it has saved over 35,000 migrants' lives in the Mediterranean Sea (Sea Watch 2019). Nonetheless, the organization has faced constant criticism from the Italian and Greek governments as well as their nationalist allies in the European Union who seek to erect a "Fortress Europe" and halt the flood of asylum seekers and refugees (Ward 2018).

Last year in Italy, right-wing bureaucrats ordered the Italian Coast Guard to stop rescuing migrants, mandating that ports be closed to migrants rescued outside the country's maritime border (Kingsley 2019). In tandem, Italian and Greek officials have threatened to launch criminal investigations against humanitarian actors and confiscate their rescue vessels. In July 2019, Sea-Watch 3, the last of the NGO's vessels, was detained by the Italian government. Its crew members face prosecution under charges of facilitating and promoting illegal migration to Europe. Meanwhile, the death toll in the Mediterranean Sea continues to climb precipitously — a "sea of blood," according to the United Nations Refugee Agency (O'Grady 2019; Tondo 2019).

This is a shocking reality. Governments are decrying humanitarian actors for rescuing drowning migrants, while policymakers continue to enact legislation that further restricts refugee access to health resources. This forces migrants into a precarious limbo where their lives depend on the whims of politicians and pundits. Above all, these humanitarian crises have challenged bioethicists and human rights advocates to consider the following:

Is health a human right?

This is a question of singular complexity, and history provides an impassioned, yet ambiguous answer. Since its founding, the United Nations (UN) has continually emphasized a fundamental human right to health. Most notably, Article 25 of the Universal Declaration of Human Rights states that "Everyone has the right to a standard of living adequate for the health and well-being of himself and his family" (United Nations 1948).

In 2005, the UN convened a committee of bioethicists and human rights advocates who emphatically upheld that notion in drafting the Universal Declaration on Bioethics and Human Rights. Article 14, titled "Social Responsibility and Health," insists that "the highest attainable standard of health is one of the fundamental human rights of every human being without distinction of race, religion, political belief, economic or social condition." Even further, it asserts that a "central purpose of governments" is to provide "access to quality health care and essential medicines" (UNESCO 2005).

What do these declarations accomplish? The answer is complicated. Many bioethicists view these treaties as unequivocal affirmations for the right to health — acts of solidarity that bind nations together in upholding human dignity and health equity (Chapman 2015). They hope that these declarations will bring a moral imperative to resolving humanitarian crises, compelling governments to enact structural change that expands healthcare access for all.

But for many, these promises have yet to be fulfilled. Some UN member states continue to infringe upon the human right to health — for instance, Italy's crackdown on rescuing drowning migrants in the Mediterranean. For this reason, some bioethicists and policymakers have criticized the notion of health as a human right as naively idealistic. In this view, human rights declarations are simply diplomatic façades, as the UN is ill-equipped to enforce mandates at the state level. (Dolinger 2016; Tasioulas 2017). For the vulnerable, rightless huddled masses, these declarations are only emblems of false hope.

In the future, humanitarian ideals of justice, equity and human rights will continue to encounter formidable challenges from the rising tides of nationalism and nativism throughout the world. From the Mediterranean Sea to the US-Mexico Border, politicians must confront the crucial question at the heart of it all:

Is health a human right?

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Interview

A Conversation with Dr. Steven Ralston

Dr. Ralston is the chair of the Department of Obstetrics and Gynecology at Pennsylvania Hospital and a Professor of Clinical Obstetrics and Gynecology at the Perelman School of Medicine. He specializes in prenatal diagnosis and high-risk obstetrical care.

Photo courtesy of Dr. Ralston

Could you tell me about yourself and your career path and a little bit about your interests?

I've been in academic medicine my whole career. I went to med school not really knowing exactly what I wanted to go into, but I fell in love with OB-GYN and that's what I ended up doing. Obstetrics was always my great love, and I became a high-risk obstetrician as my subspecialty. From that subspecialty, I sort of found my academic niche in the world of medical ethics and medical education, so I taught for many years at Tufts where I ran the core clinical clerkship in OB/GYN and then for about five years taught in their ethics and professionalism curriculum. Then I moved over to the Harvard system for about five years, where I also taught bioethics, and now I'm here at Penn.

I didn't quite have a credential to do all this bioethics thinking and teaching until I got a Masters in Public Health with a concentration in Health Law, Bioethics, and Human Rights from Boston University, and that has led to a number of other opportunities for me. I was on the Ethics Committee at the American College of Obstetricians and Gynecologists for about five years, chaired that committee for 3 years, and I've been on ethics committees in many different hospitals that I have worked at over the years. In my clinical life, I take care of women with medical problems, those who have had bad things happen to them in previous pregnancies, and women having complications in the current pregnancies. A fair amount of my clinical life involves prenatal diagnosis. This entails evaluation of fetal well-being and management of labor for patients who wind up in the hospital with medical problems impacting their pregnancies. Now, I have an administrative role here as the chairman of a very big and busy department.

Is maternal-fetal conflict common? How does it manifest, and how do you approach these situations?

So I think that there is this misconception, no pun intended, that maternal and fetal interests are somehow misaligned on multiple occasions during pregnancy. For the most part, the mothers' interests and the fetus' interests are consonant with each other. The mother's goal is to have a healthy pregnancy and a healthy baby, so she's almost always going to be making decisions that are in the fetuses' best interests if it can be said that a fetus has interests.

Conflicts arise when the mothers' interests and the interests of others around her are different, so the conflict is not between the mother and the fetus; instead, it tends to be between the mother and other people, whether it's doctors, or governments, or institutions.

In the relevant article, the author writes that pediatricians are relatively more likely to be likely to view fetuses with full rights while OB-GYNs are relatively more likely to consider them as having substantially fewer rights than the mother. Do you agree with this?

In my experience, pediatricians are, if anything, as a group, more liberal than OB-GYNs even in terms of reproductive rights. You might think that the pediatricians would lean anti-choice, but actually they are not—they tend to be a fairly liberal voting bloc with pro-choice sensibilities. Yes, their interests are about children, but when it comes to pregnant women, they usually will come down on the side of maternal autonomy. The pediatricians that I work with the most are neonatologists, and they are all about saving babies that are having complications including prematurity, but in general, those I have worked with have been very respectful and cognizant of the limitations of their desires to help babies as it impacts women's care. So they are very happy to take care of that baby when it's on the outside, but they're not going to do anything to unduly influence a woman and her decision-making. Often, when I'm working with pediatricians, it is to counsel women who are having very premature deliveries, or what we call periviable gestations in the 22 to 25 week range. Those are joint conversations with pediatricians and obstetricians in the same room with the patient so that we can counsel together, and usually, our counsel is very similar. I will say that I do think that in general, obstetricians are a little more pessimistic about what outcomes will be for premature babies compared to pediatricians who are a little bit more optimistic. The truth is probably someplace in between.

Do you believe that a doctor should be able to take legal action against expecting mothers that refuse undergoing a C-section even if that C-section is deemed necessary?

It's interesting how you phrase the question as "should doctors be able to", considering that doctors can do whatever they want. The question is, do we think it's a good medical practice for doctors to do that? And is it good public policy for us to allow such suits to go forward and to influence care? I've been doing this for a very long time, and I've never been in the situation where I've had to go to court to make anybody do anything, and I don't think I ever will. I really worry about

the underlying premise of this discussion, which implies that somehow women when pregnant either don't know what is in their best interest and so need other people to tell them or can't be trusted to make decisions that are in their best interest and in the best interests of their baby. The pregnant state should not change how we view women's civil rights.

If we let doctors decide when women should have Cesarean sections, then we should probably let doctors decide when women should take certain medications, when they should leave their job to go to the doctor's office, and when to do any list of things that in the doctor's viewpoint would make the outcome better for the baby. That's where I think the danger comes in—I think that these examples make great headlines, and I think they make great fodder for bioethics courses and in case studies, but the reality is that women make decisions that are both good for themselves and bad for themselves every day whether they're pregnant or not and the same is going to be true for their fetuses as well. Our job, I think, is to help people make good decisions for themselves, give them information, and make sure that they have enough information to make a decision. Our obligation is to help guide them somewhere we think their particular values are leading them and not necessarily where our values are leading us to guide them.

As a clinician, how does the emphasis you place on maternal autonomy influence the way you practice?

It really depends on the context, but I am an OB-GYN. I take care of women, and that lens for me has colored how I view this world. When it comes to invading somebody's bodily integrity, it's going to be very difficult for me to do that without their permission, whether that's surgery, a vaccination, an antibiotic, or a prenatal vitamin. I always think about these cases because while they almost never happen, we talk about them a lot. What would it actually look like to force women to do things that they don't want to do? It would mean that we would have to physically restrain them; we'd have to tie them down. You're not going to be able to do an operation on a woman if she doesn't want you to do it without restraining her while she's screaming at you and yelling at you to stop. If that's what a woman is saying, how does that feel as a provider? I just find it to be a diminution of who we are as clinicians to think that would be an acceptable thing to do, assuming that the woman is compos mentis.

Why do you think people focus on extreme cases that are really unusual on a day-to-day basis, like those of forced C-sections?

Learning about these extreme cases to begin with is like a laser beam, making you focus on issues of what is right, what is wrong, what is good, what is bad, what is acceptable, and what is not acceptable. I think the broader question is why do people fixate on pregnancy and women's decision-making? What women do with their bodies has been a focus of men for so long. That I think is a political question. My feeling about that is that the world has been a very safe place for men, and as women have gained more independence, have gained more rights, and threaten men's safe position in the world, the patriarchy has perceived it as very threatening and has pushed back. That's a very long story that goes back not just decades, but centuries.

You mentioned something about how much conflict in pregnancy arises not between woman and fetus but between woman and the family or other outside factors; can you expand upon that?

You can name anything, and there is potential conflict there.The woman may have a certain idea of how she wants things to go, and her partner has a different idea. So she wants to continue the pregnancy, and he wants her end the pregnancy. She wants to end the pregnancy, he wants her to continue the pregnancy. There's not always alignment between partners. Or there is a family member that is exerting influence, either wanted, needed, or undue, over what the woman may or may not want.

Then there are institutions that really restrict what choices women have. Say I'm a woman and I come in and I have a miscarriage, and I'm at a Catholic institution when I have that miscarriage. I inquire, well, what can you do to help me prevent the next pregnancy? And they say, well, we're a Catholic institution. We can't do anything to help you prevent the next pregnancy except tell you to not have intercourse. But if you want birth control, you have to go to a different institution because in our institution, we restrict those options for you. Or you might be at an institution where a woman wants to get her tubes tied after her delivery, and she has Medicaid. But Medicaid requires a woman to sign a form thirty days before she has her tubes tied, and she hasn't signed those forms. So she isn't able to access that care because of an institution: the federal government, hospital, state, or whatever it is putting those restrictions on her. So in these cases, the conflict is not between the mother and the fetus, it is between her and the world that is creating conflict.

What options do physicians have; how do you respond to such cases?

It depends on what those situations are. Certainly, when it's individual family members that seem to be problematic, then you try to separate the mom from those individual family members so you can really get a good idea of what she herself is interested in and wanting. If it's institutional barriers, then we work within our institutions to try to change those barriers. If the reason my patient can't get her IUD is because our hospital doesn't stock those IUDs, I'm going to work through our purchasing people, our pharmacy, and our administration to say, "We should stock the IUDs so our patients have access to them." If it's a government, you have to lobby, you have to advocate, you have to vote; all those things to push legislation to make change in society.

A Conversation with Dr. Jennifer James

Dr. James is an attending neonatologist at the Children's Hospital of Philadelphia. She has published articles on neonatal resuscitation and discussions about withdrawal of life support for preterm infants.

Photo courtesy of Dr. James

Could you tell me about yourself and your career path and a little bit about your interests?

I did my residency and fellowship here at CHOP, and I've been an attending here for a little over three years. I'm currently the Associate Medical Director of the Intensive Care Nursery at HUP. One of my main interests is communication with families, so I do a lot of teaching with our NICU fellows about delivering serious news and communication regarding goals of care. One of my main roles here at HUP is that I am the neonatal physician liaison to the MFM department, so I am the neonatologist that they talk to when we have complex patients to manage with both maternal and fetal issues. I do outpatient consults for any mothers carrying fetuses who have congenital anomalies, severe growth restriction, or who have a medical problem that could impact the care of the baby, such as maternal malignancy or cardiac disease. I meet with these mothers prenatally to review expectations for the delivery and neonatal course and I discuss delivery planning with their Maternal Fetal Medicine physicians.

Is the prenatal consult standard for all mothers, or is it just when they've identified something that needs special attention?

It's just when they've identified something that would require special attention. If the baby has congenital heart disease, congenital diaphragmatic hernia, a myelomeningocele, or some other significant anomaly that we know is going to require specialized care immediately after birth, I meet with the family to explain how we're going to take care of and support the baby and then what the hospitalization might look like. And then sometimes it's more about decision-making. For example, if the fetus is severely growth-restricted, we talk about what gestational age might it make sense for the OBs to start testing. That's something the OB and MFM physicians counsel the mothers on all the time, but sometimes in order for the mother to make that decision, she needs to hear from a neonatologist. So I talk to them about what prematurity at a particular gestational age and size would look like and help them make decisions together with their MFM about how aggressive they'll be with testing.

How do you reconcile goals of care for mother and fetus?

They're really tied together. While it is the obstetrician's and maternal-fetal medicine physician's job to protect the interest of the mom, we of course support that as well. I think it's not as simple as saying "The OBs look out for the mom's, and the neonatologists look out for the baby's well-being", I think we're all in it together, and for the vast majority of cases, the mom and the baby's interests are aligned. The mom wants what's best for the baby, and the OBs also want what's best for the both mom and for the baby. In most cases, those views are aligned and actually many times mothers are willing to take on substantial risk to themselves in order to provide even a small benefit to their baby. I think it's the rare circumstance where those interests appear to not be aligned. And that's difficult.

Have you encountered that before? What do you think of forced C-sections?

Yes, I have. One example is when the fetal heart tracing during labor doesn't look reassuring, which is an indication that the baby is in distress. And the obstetricians, based on their experience and the standard of care, recommend a C-section to optimize the chance of a good neonatal outcome, a healthy baby. A mom might say, "I don't want a C-section; I don't want that to happen to my body, I think the baby is going to be fine." Most ethical frameworks state that the mother's rights and her autonomy should not be diminished just because she's pregnant. But the question of the rights of the fetus is really complex. What's our moral obligation to the baby?

I think that on the surface level, if you ask a neonatologist they'd say of course we should do everything we can to get the baby out as healthy and safely as possible. But if you actually delve deeper, I don't think that many people would consider it ethically permissible to force a woman against her will to undergo a major surgical procedure. Yes, we neonatologists have babies' best interests in mind, but at the same time, we respect the mother's rights. Women are not just vessels. I think it's really important to acknowledge that just because they are pregnant, it does not diminish their autonomy to make medical decisions. It's very ethically complex when you actually talk about forcing care onto a person, and I think as a woman myself, that is a really scary thought.

I think the answer is not in court orders but rather in communication and multidisciplinary collaboration and approach. Both the OBs and the NICU doctors go in and talk to the family together to hear their reasoning, what they're worried about, and to convey the risks of not having a C-section. OB especially is very good at ultimately getting moms to where they need to be and having them understand that we want what's best for both Mom and baby, without

getting courts involved. I think that obtaining a court order is really detrimental to trust in the physician-patient relationship, and I think it should really be avoided at all costs. There's already a lot of pervasive distrust that our patients have of the medical community, and I think if at all possible, those conflicts should try to be resolved with just more communication and time spent with the family, trying to understand where they're coming from and why they're making these decisions.

You've talked a lot about respecting patient autonomy and values, but do you think there are instances where it is advisable for the physician to give recommendations that push those values a little?

Yes, I think in general my approach is to figure out their values, what's important to them, and to say, "Based on what you're telling me, I think this is the path we should take." However, there are times I am a little more directive and I think we owe that to them - to shoulder some of the decision-making burden. I also think different families need different things. Some families or some cultures might need a more paternalistic approach or a more recommendation-heavy approach, while others would be very turned off by that style.

I think it in general decision making should be family-centered, but it should not be menu-based. I think you should still elicit their goals and then give your recommendation to them based on their values, not based on your values. I think that it's really hard but very important that physicians keep in check what is the actual medical data and evidence versus what is their own biased and value-laden opinion. As well, I think it is important that we keep ourselves up-to-date on the latest data because outcomes for premature babies ten-twenty years ago are different than they are now, and you can't be quoting the old outcomes.

What are some challenges you've encountered in interspecialty collaboration?

I would say that at least here, at this institution, we have an excellent collaborative relationship between neonatology and maternal fetal medicine. There are plenty of times where we've had tough cases; we've had cases where if a mom who's pregnant has a terminal illness, and we ask, can she be a DNR if she is carrying a viable fetus? That's a very complex issue because we all want to respect the wishes of a dying woman, but we also have to determine what is also in the best interest of the baby.

More commonly, we'll have a baby with an anomaly, such as congenital heart disease, and a mother has a complication, such as preeclampsia. We know for the mom's safety, she should be delivered, which is the definitive treatment for preeclampsia. If she isn't, the disease could progress and be life threatening. But if a baby with a significant heart defect is too premature, that baby would not survive if delivered early. In these cases, we've had to talk to each other and make collaborative decisions. The MFM physicians might expectantly manage her a little while longer than they would normally do if the baby didn't have heart disease and talk about what risks are they willing to take for the mom in order for her to be able to get the baby to an age where the baby could survive outside the womb.

I think any discussion around the limits of viability are complicated because they represent our gestational age range that we think is the earliest a baby could survive outside the womb. So at this institution, we consider 22-24 weeks this grey zone where the majority of babies, especially at 22 weeks, will die, and if they survive, have significant developmental or medical morbidities. Whenever a mom presents at these gestational ages, it's a collaborative discussion with OB and NICU about how are we going to best take care of Mom and baby together and support the parents' wishes. There is very complex decision-making that has implications for both mother and baby; we talk about fetal monitoring during labor as well as what C-section would mean for this mom at this gestational age.

What strategies do you have for mitigating differences between OB and neonatology?

I honestly think bringing it back to the family and the family's goals is important because family-centered decision-making should be the hallmark of all of these complex decisions. So I think as long as we are sure that in collaboration we have presented all the information to the families about the risks and benefits of certain tests or interventions or delivery plans, and explored their values, then we need to respect what they choose. Their decision might be different than what we individually might value or think we would choose ourselves, and it's important to be mindful of the way our own beliefs influence our counseling. If we as an institution have determined what interventions we think are reasonable to offer, and the family is choosing one of those interventions, even if it's different from what we think would choose, then we need to respect the family's decision. I think that's the best way to talk about it when there are different disciplines and different people with various opinions.

Do you think it's a good thing for fetal care teams to have both the OB and neonatologists' perspective?

Yes, 100 percent. I think it's critical. I think in general, we have a really good model of that here. For any kind of complex situation where the mother has a complex medical problem that might affect the course of the pregnancy or if the baby has anomalies that will affect decision-making and affect the care of the baby afterwards, I think it's really critical that OBs and neonatologists are working together. I think it's important to hear the other person's perspective because you might say, "Oh, we think this is what's best for the baby," and the OBs can say, "But remember this, that part isn't going to be good for the mom," reminding each other we need to think about both of them together. Both of us want the best for the mom and the baby. If people are thinking in tunnel vision, neonatologists will of course want everything to be optimized for the baby, but no one actually only thinks about that. We want the best outcome for the two together, and I think that's true for MFMs physicians as well.

Article

Who Forced the C-Section? Maternal-Fetal Conflict and Different Objectives of Care

Tarika Srinivasan*

With the birth of gene-edited twins in China, scientific backlash has fueled an urgent need for new governance. Overstepping of ethical boundaries demands a revisiting of regulatory policymaking and a renewed deliberation on clinical genome editing and its applications through a new or modified international framework. Fundamental questions encompassing our ability to control human evolution serve as a backdrop for quandaries regarding multigenerational consent, genetic correction versus enhancement, societal and social implications, religious considerations, moral obligations, and human welfare. As clinical genome editing has immense potential to eradicate disease, it should certainly be an option; however, the questions of which cases it should be allowed in, what legal framework is needed to regulate these cases, and who makes these decisions as part of an international committee must by driven by the public and all stakeholders.

Introduction

Physicians are often baffled by pregnant patients who refuse a medical treatment on personal, religious, or sociocultural grounds. Cesarean sections are sometimes prescribed as a surgical alternative in cases where natural delivery may be contraindicated for the child, such as breech presentation, HIV infection of the mother, or fetal birth defects. There have been a substantial number of cases in which pregnant women have refused to undergo C-sections even after their physician has confirmed the necessity of the intervention as life-saving for the fetus. As a result, some physicians have gone far enough to seek legal action against the mother for endangerment of the child, via a court-mandated C-section. This practice has further characterized maternal refusal of medically indicated C-section as potentially criminal behavior (Miller 2005).

Fetal care may fall under the purview of an obstetrician or a pediatrician. While both specialties might be expected to carry out medical care in tandem, their views of the maternal-fetal relationship are fundamentally different. As a result, pediatricians and obstetricians can be expected to approach maternal-fetal conflict from opposing angles, translating to separate outcomes based on specialty. In regards to legal intervention, pediatricians might be more likely to pursue court orders against mothers for refusing C-sections, while obstetricians often respect the mother's autonomous choice (Brown et al. 2006).

This paper asserts that the objectives of care of these two specialties translate into conflicting views on forced C-sections (by legal or coercive means). Because medical care of the maternal-fetal dyad necessitates intrusion on and risks posed to the mother, prioritizing fetal intervention against the autonomy of the mother is generally condemned by the wider medical professionals outside of obstetric and pediatric professionals (Arora and Salazar 2014). The paper will give an account of fetal rights per both specialties and the historical views of each on forced compliance; a discussion of outcomes of specialty-based conflict and possible remediation will follow. In accordance with accepted principles of professional medical ethics and federal law, I argue that the subversion of maternal autonomy in the interest of the fetus is fundamentally damaging to the physician-patient relationship and should be critically examined before pursuing legal intervention.

Maternal Refusal of C-Section

The Cesarean section continues to be the most common surgical procedure performed in the United States; the procedure exceeded 1.2 million cases in 2018, comprising 32.0% of all deliveries (Martin 2018). This high rate has been a cause for concern for health care professionals and patients alike, as electing to deliver via C-section even for low-risk pregnancies has become somewhat commonplace. The most common reasons for Cesarean section include stalled labor, fetal distress, transverse or breech fetal positioning, or mechanical obstruction, such as a fibroid, pelvic fracture, or placenta previa (Mayo Clinic 2018). In these cases, the procedure is medically indicated to maximize healthy delivery of the child, though there may be limited direct benefit and additional risks to the mother. Standard risks include infection, postpartum hemorrhage, blood clots, surgical injury, and increased chance for serious complications in future pregnancies (Mayo Clinic 2018). Furthermore, mothers who deliver via C-section tend to express less immediate and long-term satisfaction with the birth, are less likely to breastfeed, and tend to experience more difficulty bonding with infants postpartum (DiMatteo et al. 1996).

These physiological and psychosocial risks may themselves cause a woman to refuse a C-section when

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the procedure is medically indicated. Language and cultural barriers may further aggravate the issue, as health professionals may not be able to adequately obtain consent, convey safety measures, or address patient fears. Women belonging to ethnic or religious backgrounds that place value upon having several children may feel particularly worried about C-sections posing a threat to future fertility and delivery. Finally, hospital charges for C-section are nearly twice as much as that of vaginal delivery, which might further disincentivize women to consent to the procedure (Deshpande and Oxford 2012).

While the incidence of published cases of maternal refusal of C-section is quite low, attorneys attribute this to the relatively high bar of entry for such cases into the legal system rather than low occurrence itself (Morris and Robinson 2017). Advocates and attorneys indicate that coerced and forced C-sections occur frequently within hospitals, but the relatively low percentage of documented court orders for C-sections obfuscate the estimated rates of maternal refusal. Because the physician court order process is additionally time-consuming, delay in obtaining approval further increases the risk of both maternal and fetal morbidity and mortality (Deshpande and Oxford 2012). Thus, physicians may elect to take medical decision-making into their own hands and seek retroactive court approval after proceeding with C-section against maternal wishes. This circumvention of the patient's wishes can often be experienced as trauma and bodily assault, as indicated by a qualitative study of birth trauma and PTSD symptoms in postpartum mothers (Reed et al. 2017). Thus, not only does coerced C-section significantly damage trust in the physician-patient relationship and the overall health system; mothers may experience post-traumatic symptoms that further affect delivery recovery and postpartum bonding with the infant.

Fetal Moral Status and Objectives of Care

There are three primary perspectives concerning fetal moral status. The fetus may be regarded as having the full rights of a child, no rights at all, or increasing rights with advancing gestational age (Isaacs 2003). A fetus given full and equivalent rights as a child is considered a morally significant entity separate from the mother. This is reflective of the shift of the medical model of the biological maternal-fetal relationship from united dyad to separate patients (Fasouliotis and Schenker 2000). This model is inherently problematic due to fetal dependence on the mother. Fetal diagnosis and therapy inevitably rely on access to the fetus via the pregnant woman. Frequently, the pregnant woman agrees to undergo interventions for the sake of the fetus. However, in those few cases where the pregnant woman does not, there is a serious conflict of rights between fetus and mother. Some argue that the fetus has no moral status independent of the mother and only acquires such at birth (Isaacs 2003). Assuming no rights for the fetus strengthens maternal autonomy. Court-ordered interventions are thus never justified, as the only patient's risks and benefits that come into the equation are the mother's. Once a pregnant woman has made an informed decision to refuse a treatment, there must be complete acceptance of her decision by the medical team. Increasing rights with advancing gestational age alters the moral status of the fetus progressively (Isaacs 2003). Early termination of a pregnancy may be permissible without consideration of fetal rights while a late-term intervention (such as a Cesarean section) may be evaluated based on consideration of both mother and fetus.

Biomedical ethics emphasizes the use of moral principles to apply general ethical theories to problems of therapeutic practice, health care delivery, and medical research. The four principles of biomedical ethics, as put forth by Beauchamp and Childress, are autonomy, beneficence, non-maleficence, and justice. In considering these principles in problems of maternal-fetal conflict, if full rights are given to a fetus, the autonomy of the mother clashes with the beneficence to the fetus. This right to autonomy of the woman can be interpreted as the right to choose how to live one's life (Isaacs 2003). R. v. Morgentaler, 1988 established the legal right of the pregnant woman to be free from unwanted bodily invasions, as an extension to the right to security of the person. Men and non-pregnant women have generally been granted the right to refuse medical treatment based on personal volition. By this measure, one may conclude that the pregnant woman has full freedom to choose the mode of therapy based on their personal values and beliefs.

The principle of beneficence requires the physician to act in provision of more good than harm towards the patient's life (Fasouliotis and Schenker 2000). In giving the fetus full rights in maternal-fetal relationships, the physician is responsible for providing a greater benefit than risk to both mother and child equally. This dual obligation understandably puts the physician in a difficult position. A one-patient model allows the physician to evaluate maternal-fetal benefits and risks as a total, whereas a two-patient model may not warrant a single treatment for both patients on beneficence principles alone (Tran 2004). The burdens on one patient (i.e. the mother) may not be balanced against the benefits for another (i.e. the fetus).

These differing views on the fetal moral status are reflective of two different objectives of care. Obstetricians generally tend to view the maternal-fetal relationship as dyadic, with the fetus having substantially fewer to no rights compared to the mother. The mother's informed choice to refuse a treatment is often honored by virtue of her autonomous decision-making. On the other hand, a pediatrician may approach the fetus as having full rights, or at least increasing rights (Rink 2012). The pediatrician may therefore place additional weight on any proposed intervention to benefit the child. These differences in views on fetal rights form conflicting objectives of care; obstetricians approach maternal well-being as paramount

while pediatricians additionally emphasize fetal outcome.

Objectives of care can and have been connected to differing outcomes in the treatment of medically similar obstetric cases. For example, a study of counseling after prenatal diagnosis of a fetal condition (e.g. trisomy 21, spina bifida) showed that obstetricians were more likely to refer the patient to fetal termination services, while pediatricians often instructed the patient to follow up with counselors in pediatric specialized care instead (Brown et al. 2012). Similar studies depict this emerging pattern of obstetricians and pediatricians favoring maternal or fetal focus, respectively, in prenatal care. Obstetricians often lack knowledge about post-birth outcomes and medical management of children with complex disorders. Treatments proposed by obstetricians skew toward fetal termination and/or preferences of the mother (Rink 2012). Consider the management of a patient who is vehemently opposed to C-sections and is pregnant with a child who has a complex breathing disorder. Suppose that the pediatrician has some experiential knowledge to hypothesize that a C-section could result in better survival of the neonate. The pediatrician may then go so far as to attempt to coerce or obtain a court mandate for the woman to undergo a C-section, while an obstetrician, after presenting adequate information to the patient, may accept the woman's autonomous choice.

Medical Professional Associations on Forced Compliance

Obstetricians, including fellowship-trained maternal-fetal specialists, have served as the predominant health care providers for pregnant women. As fetal interventions have grown increasingly sophisticated, the American Academy of Pediatrics (AAP) has advocated that pediatric specialists be directly involved in fetal care, especially in medically complex cases (Brown et al. 2006). The question arises whether management of fetal cases by pediatricians will prioritize the interests of the fetus over those of the mother.

Historical bioethical proceedings of the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP) are subtle evidence of the effect of professional training and affiliation on attitudes toward maternal-fetal interventions. These differences are evident in the organizations' prior statements on fetal therapy, released by the AAP in 1999 and ACOG in 2004. The AAP seemed to permit more challenges to maternal decision-making amongst its practitioners, recommending that physicians emphasize the mother's "responsibility to accept some personal risk for the potential benefit to her fetus" if the mother were to refuse a proven fetal treatment (AAP 1999). The AAP furthermore stated that if the intervention is deemed necessary, the physician is not only warranted but compelled to pursue judicial authorization as a last resort. The ACOG, meanwhile, accepted the woman's ethical obligation to promote fetal wellbeing, but stopped short of assigning a responsibility to assume personal risk for the fetus. They concluded that judicial authorization may be warranted in extraordinary circumstances, but even in those cases, the physician is still discouraged from physical intervention against the mother's wishes, even with a court authorization in place (ACOG 2004).

Since both of these statements, there has been some collaboration between the organizations to release more congruent opinions on judicial authorization. A later joint statement from both organizations discouraged the pursuit of court authorized intervention, acknowledging that the woman's right to refusal be fully respected (ACOG and AAP 2011). Yet some differences in professional rhetoric remain. Pediatric and obstetric perspectives repeatedly differ in regards to maternal decision-making and autonomy. The ACOG regularly emphasizes the psychosocial consequences of court intervention, including loss of trust, discrimination against cultural minorities, and compromise of individual liberty (Sacks & Koppes 1994). In reaching an impasse on maternal-fetal conflict resolution, the ACOG suggests re-evaluating the physician's convictions and transferring care to another specialist; the AAP fails to recommend either.

If the statements of each of these associations are taken to be reflections of general professional attitudes, there are clearly some differences in willingness to challenge maternal decision-making between specialties. It should be noted, however, that neither the ACOG nor the AAP are regulatory bodies. Neither have the power to make policy changes or substantially punish physicians for actions deemed out of line with their ethical proceedings. Obstetricians and pediatricians have full authority to seek court intervention despite recent discouragement from their respective peer bodies. Thus, the statements of each organization's ethical committees may be interpreted as some ideal that exists amongst the members of the professional community. Their power to sway physicians' decisions should be regarded more skeptically.

Outcomes of Differing Objectives of Care

Through the 1990s and early 2000s, cases of court-ordered C-sections were quite numerous. After being forced by judicial authority to undergo C-sections, patients often filed to appellate courts (Glezer 2018). The corresponding judicial rulings in the appellate cases were often overturned; the interventions were sometimes even ruled to be violations of bodily integrity and tantamount to battery (Townsend 2012). Today, the pursuit of court-ordered interventions against patients is heavily discouraged in the medical community, but has still been successful in lower courts. Physicians and hospitals otherwise manage to avoid the legal hurdles of court orders by coercing patients to agree to C-sections. These parties have been documented to engage in such coercion by denying patients further medical care, labeling patients as non-compliant, and threatening to call Child Protective Services (Morris and Robinson 2017).

These practices are in clear violation of the autonomy of the mother, as a patient who has the right to refuse medical treatment. While physicians and hospitals may attempt to force a woman to undergo C-section for a variety of reasons (including fear of malpractice lawsuit after vaginal delivery and better maternal outcome), those cases in which the C-sections are recommended by the doctor to ensure fetal outcome fit under the broad umbrella of maternal-fetal conflicts.

Most medical ethicists condemn the pursuit of court interventions against mothers refusing treatment for the sake of the fetus (especially C-sections). Early perspectives opposed even recognizing any fetal rights that could create an adversarial role between the mother and child. While it was noted that a woman in late-term pregnancy may have an ethical obligation to accept treatment for the sake of the fetus, the prevailing opinion was that this obligation should not be legally enforced. Treatment of the fetus was thus insufficient reason to take action to override the autonomy and self-determination of the mother (Nelson and Milliken 1988). For example, a mother could not conceivably be court-mandated to assume the risk of organ transplantation to donate a kidney to their child, even if medically necessary.

Despite this overwhelming discouragement, the practice of seeking court authorization for intervention has prevailed amongst physicians and hospitals. Some assert that this is mostly a regional trend correlating with pro-life action in conservative states with an interest in protecting fetal life (Isaacs 2013). Utah was the first state to press criminal charges against a mother who refused a C-section after she gave birth vaginally. The basis for the ruling derived from prosecution of women for drug use during pregnancy (Miller 2005). This leap from court authorization to criminalization of C-section non-compliance has been largely denounced, with ethicists advising that physicians not confuse moral with legal obligations.

Just as regional political thought has shaped trends of forced compliance with C-sections, individual physicians' political views may be correlated with pursuit of court authorization as well. A study of physicians identifying as Democrats or Republicans showed that each group tended to give different care recommendations in politically divisive issues, including those surrounding pregnancy and fetal termination (Hersh and Goldenberg 2016). Another study of fetal care providers in particular revealed that situational differences of a non-compliant mother significantly affected propensity to pursue a court order for C-section: drug use by the mother was positively associated, while diagnosis of the fetus with trisomy 21, religious objection, and paternal refusal of C-section were negatively associated. Most notably, the physician's identification with "pro-life" ideology was consistently associated with their likelihood to pursue a court order for C-section (Samuels et al. 2007).

With this sustained evidence of action against maternal autonomy, it is clear that the professional discouragement of court authorization has been overshadowed by individuals' political opinion. Ultimately, this may stem from a lack of set objectives of care in the maternal-fetal relationship. To summarize the development of the problem, differing views on fetal rights and interventions amongst obstetricians and pediatricians have created a jumble of thought amongst fetal care providers in which no standard protocol has been set to address maternal refusal to undergo C-section. Physicians develop and strengthen opinions on the permissibility of court authorization during specialized training, falling into patterns of action in regards to maternal autonomy (Rink 2012). Political opinion further reinforces viability of court authorization, creating the subcultures for and against legal intervention in maternal-fetal cases observed amongst pediatricians and obstetricians, respectively.

Recommendations for Resolution

Based on the outline of the issue above, the most critical step to remediation is the establishment of a nationally shared directives of care during maternal-fetal conflicts within all sectors of the medical community. Of course, this will not be easily achieved. While pediatricians and obstetricians have come together to author joint opinions on the subject, ending the pursuit of court authorization amongst physicians requires cooperation much earlier in the medical career. Joint education of pediatricians and obstetricians with medically complex cases warranting fetal intervention may encourage collaboration between these two typically divergent communities. Throughout medical education, the autonomy of the patient to refuse treatment, regardless of that patient's status as pregnant, must be emphasized. This creates an unwavering stance on patient rights, strongly discouraging any legal action that may undermine them.

Consultations with medical ethics teams in these cases are crucial, so as to discourage paternalistic action against maternal patient autonomy. The objective of physicians should be to convince, rather than to coerce, the mother to undergo C-section when medically indicated for the benefit of the fetus. Involvement of social workers, translators, chaplains, and counselors may be useful to address the patient's religious, sociocultural, or psychological objections to the intervention. Physician action protocols for refusal of medically indicated C-section have been developed and tested to varying degrees of success (Deshpande and Oxford 2012). Training of medical students and residents to use these protocols is imperative in setting standard ethical practices amongst differing specialties, with legal intervention discouraged across the board.

Practicing physicians and medical groups who have sought out court orders or coerced patients to undergo C-sections must be adequately addressed. Gender bias and discrimination have often been identified as root causes for physicians' efforts for forced compliance against mothers (Townsend 2012). Furthermore, nearly 80% of cases of legal action against non-compliant mothers have involved

patients belonging to religious or cultural minorities (Glezer 2018). Education focusing on implicit biases (perhaps via ethics training modules) may help to ensure that cases of forced compliance are minimized.

Finally, fetal care teams, especially for medically complex cases, should be amended to include both obstetric and pediatric personnel. Outcomes of fetal care vary greatly based on the specialty of the handling physician, sometimes to the detriment of the patient's personal autonomy. The establishment of an obstetric-pediatric team may create a collaborative relationship between medical personnel and patients with one unified set of goals and care approaches throughout the duration of the pregnancy. Early enrollment of patients with such care teams in their pregnancy, before conditions warranting fetal intervention are diagnosed, may proactively reduce the potential for maternal-fetal conflict. Both physicians might go over the objectives of maternal-focused and fetal-focused care early on, explaining to the patient situations in which conflicts may arise. With this information, the patient may choose a preferred direction of care, thereby setting patient-directed objectives for medically indicated intervention before the maternal-fetal conflict occurs.

Conclusion

The medical community reflects different views of the maternal-fetal relationship amongst pediatricians and obstetricians, with emphasis on fetal rights or maternal rights, respectively. Conflict between the mother's autonomy and fetal beneficence for medically indicated interventions such as C-section, is therefore inevitable. Specialty training and political opinion further widen the divide, enabling forced compliance of the non-compliant mother via coercion and legal intervention. Such practices undermine the autonomy of the mother, as a patient who has the right to refuse treatment and is not legally required to assume risk for an intervention for their child's benefit. Collaboration amongst pediatricians and obstetricians to set a unified protocol of care in maternal-fetal conflicts may ameliorate the continued practice of legal intervention against patients. Counseling patients early on with interdisciplinary care teams may set patient-directed objectives that address personal concerns and minimize non-compliance with medically indicated fetal interventions. With a renewed emphasis on patient rights and autonomy, maternal-fetal care is yet another discipline reflecting the widespread call for holistic, collaborative care models in medical practice.

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Article

Hubris or Helpful? Ethics and governance in heritable genome editing

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With the birth of gene-edited twins in China, scientific backlash has fueled an urgent need for new governance. Overstepping of ethical boundaries demands a revisiting of regulatory policymaking and a renewed deliberation on clinical genome editing and its applications through a new or modified international framework. Fundamental questions encompassing our ability to control human evolution serve as a backdrop for quandaries regarding multigenerational consent, genetic correction versus enhancement, societal and social implications, religious considerations, moral obligations, and human welfare. As clinical genome editing has immense potential to eradicate disease, it should certainly be an option; however, the questions of which cases it should be allowed in, what legal framework is needed to regulate these cases, and who makes these decisions as part of an international committee must by driven by the public and all stakeholders.

Introduction

CRISPR-mediated gene editing of human cells falls into three categories: (i) somatic gene-editing (editing in non-reproductive cells), (ii) germline gene editing for research purposes, and (iii) heritable genome editing to create a genetically modified human, where such modifications are passed on to future generations. With the surge in genome modification success, the ever-expanding biotechnology toolkit, and advances in sequencing technologies, this paper will explore the prominent and controversial topics stitched into heritable genome editing.

Following the first in vitro use of genome editing in human embryos (Liang 2015), the First International Summit on Human Gene Editing convened in 2015 to discuss the social and ethical questions surrounding somatic and germline genome editing. This meeting included the U.S. National Academies of Sciences, the Royal Society of the United Kingdom, Engineering, and Medicine, and the Chinese Academy of Sciences. The meeting concluded that any clinical germline gene editing "would be irresponsible … until (i) the relevant safety and efficacy issues have been resolved … and (ii) there is broad societal consensus about the appropriateness of the proposed application" (National Academies Press 2015).

In November 2018, the Second International Summit on Human Gene Editing convened on the back of the announcement that Chinese biophysicist, He Jiankui, had used CRISPR-Cas9 to disable the gene CCR5 in IVF embryos in order to endow HIV immunity (Jing-ru 2019). His actions resulted in the birth of twin girls. While many papers describe the ethical shortcomings of He's work, the more fundamental question surrounding the scientific and social acceptability of heritable genome manipulation has begun to garner the attention it demands.

Heritable Genome Editing (HGE)

Heritable genome editing is the modification of heritable DNA (i.e. in sperm, eggs, or embryos) which results in the birth of a genetically modified child (Lander 2019). The spread of the genetic edit to future generations can only be halted if all carriers ceased to have children or an additional genetic procedure were utilized to undo the initial modification. HGE has the potential to eradicate inherited genetic diseases that have plagued family lineages, to decrease the likelihood of developing a certain illness or disease, and to enhance human capabilities (Coller 2019).

Coupled with preimplantation genetic diagnosis (PGD), in vitro fertilization (IVF) enables couples with knowledge that they are at risk for transmitting a disease-causing genetic variant to screen for and select a non-diseased embryo for implantation. Sperm, egg, or embryo donors are other options if the couple is accepting of a partially or fully biologically unrelated child.

Although these alternatives exist, there is still a case for heritable gene editing. First, IVF with PGD is not always successful, largely due to an inability to gather a viable, disease-free embryo that successfully leads to a successful birth. PGD heavily decreases the number of embryos available for transfer since a portion of embryos carry the undesired disease genotype and others cannot be tested due to poor quality after in-vitro development (Steffann 2018). Second, HGE may be preferable in treating polygenic diseases, which IVF with PGD cannot screen against (Gyngell 2017). However, the inherent complexity of non-Mendelian traits and risks associated with modifying these interactions limit our ability to correct polygenic disease and/or enhance polygenic human characteristics. Third, HGE is the only option for the small fraction of couples whose parental genotype

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will result in one hundred percent of embryos having the disease genotype to bear a fully biologically-related healthy child. This last case is, perhaps, the most defensible and promising application of HGE.

If HGE does eventually become a proven standard technology for creating desired edits to heritable DNA, techniques such as IVF with PGD could be rendered obsolete as there will be little reason to produce a surplus of embryos. Thus, there is also the question of whether HGE is only ethically acceptable if no other reproductive interventions are available, particularly if it is assumed that HGE is 100% safe and efficacious.

Safety and Efficacy

Currently, genome editing technologies carry relatively high risk of unintended off-target edits, which, depending on the genomic location, could cause disabilities, defects, and other diseases such as cancer (Kim 2015); however, improvements to the technology will make this a non-factor in considering the use of HGE. CRISPR-induced mosaicism is another technical problem whereby only a portion of cells in an embryo are successfully edited (Yen 2014). As a potential alternative to avoid mosaicism, gamete-precursor editing and expansion, could be used. While this has been successful in mouse models, it has never been done in human cells.

With these safety concerns, informed consent is a key ethical stipulation. Regarding HGE, informed consent does not merely apply to the parent of the child being edited or the child itself but all future descendants of the edited child. Thus, it is impossible to obtain such consent from the parents and children of non-existent generations. This is a new bioethical territory that has yet to be explored. New discussion is necessary in order to create a framework for multigenerational consent (Coller 2019).

Genetic Correction and Enhancement

In and of itself, HGE and genome editing technologies are not the primary focus of bioethical debate. The applications of HGE are the points of contention. Genetic correction refers to the editing of "a rare mutation that has high probability of causing a severe single-gene (Mendelian) disease" (Lander 2019) and could eliminate genetic disease variants from the gene pool permanently. The list of disease cases for which HGE-mediated correction is approved and the procedure for a disease case to be added to this list is not yet clear. Discussion at an international scale with all stakeholders, especially those affected by the disease in question and their caregivers, is crucial if genetic correction by HGE is to move forward.

Genetic enhancement, however, is much more controversial. Furthermore, the expansion of the "combating disease" definition by the U.S. National Academy of Sciences (National Academies Press 2017) and the Health Council of the Netherlands (COGEM 2017) to "prevention of disease" presents a confounding predicament. For example, the protein Klotho has been successfully upregulated in human cell lines via gene editing to prevent neurological demyelination and associated degenerative neurological disorders (Chen 2018). However, Juengst and colleagues point out that "upregulating the Klotho gene has also been shown to enhance cognition in mice and to increase murine life-span by as much as 30%" (Juengst 2018). Therefore, genome editing to modify disease risk in a healthy individual may have enhancing effects. Moreover, modifying disease risk for one disease could increase susceptibility to other diseases (Falcon 2015). Understanding the pleiotropic effects of preventative gene editing intervention will require extensive and continuous research.

In polygenic diseases and traits, HGE may never find full support due to our minimal understanding of the vast complexity of gene-gene and gene-environment interactions and their associated risks. However, proponents of HGE point to the fact that it could be used in polygenetic applications, such as intelligence, to shift people's polygenetic scores into a favorable range. Using polygenetic scores to enhance intelligence would be based on variants already existing in the human population and thus represent "normal range human enhancement" (Gyngell 2019, Kahane 2015). While this type of enhancement might prove plausible, the complexity of polygenetic traits still comes with unknown risks.

Societal & Social Implications

Perhaps the largest ethical quandaries lie in the societal and social implications if HGE is successfully implemented on a wide scale. It could strengthen already existing stigmatization and discrimination against people with genetic disabilities. Additionally it could lead to the commodification of children (Ishii 2017); parents could be looked down upon for not genetically "fixing" a child with a certain disease; a parental genetic arms race could ensue; inherent social and biological inequalities could be worsened due to unequal access to the technology (Baylis 2017); permanent, harmful effects on our species could result from our attempt to control evolution; or human subspecies could be created (Lander 2015).

In contrast, proponents of HGE state that these arguments are pure speculation and extravagantly unlikely since current regulatory frameworks could be adapted to include regulations on HGE (Gyngell 2017). Additionally, unequal access is not a problem solely for HGE, but also for other goods such as education. This issue is not a reason to ban HGE, but instead an opportunity to ensure responsible development that maximizes accessibility (Gyngell 2019). Furthermore, the claimed negative consequences for future generations can be mitigated or

avoided altogether. Some take a utilitarian viewpoint, asserting that there is a moral obligation to pursue HGE since doing so would overall decrease human suffering and increase human welfare (Harris 2015). Gyngell and colleagues argue that this obligation is linked to intergenerational justice (Gyngell 2019, Powell 2015). Harmful mutations build up in the population as modern medicine retains these genetic variants in the population gene pool. Using environmental ethics, Gyngell claims that HGE is a compensatory action so that future generations can "enjoy the same level of genetic health as we enjoy today."

Religious viewpoints add to the complexity of HGE's application. Several religions voice the proponents' argument of a duty to protect against human suffering and emphasize the importance of having children. Thus, utilizing HGE to cure and protect against a fatal disease can be supported from certain religious perspectives, particularly when that disease causes infertility (Coller 2019). However, when using HGE for enhancement, its case is much more difficult to support. The concept of "playing God" or "meddling with God's creation" also factors into religious views on HGE. Views on what exactly is defined by these phrases differs between different religions and those involved within these belief systems.

Conclusions

As of 2017, many statements outline different groups' stances on germline genome editing for both research and clinical use. Ormond, et al. present a well-organized summary of the statements from The Hinxton Group, the NAS/NAM/CAS/UK Royal Society International Summit, the NAS/NAM Committee on Human Gene Editing, the ASGCT and JSGT, the ISSR, Baltimore, et al., the EGE, Lanphier et al., the ACMG, the NIH, and the HFEA. The researchers note that most statement restrict use of HGE and its goal to make a genetically modified child (Ormond 2017). In the latest developments, two international committees have been formed: (1) WHO expert advisory committee on Developing global standards for governance and oversight of Human Genome editing (2) The International Commission on the Clinical Use of Human Germline Genome Editing. Both bodies will report on their findings in the Spring of 2020.

Given the potential to cure diseases that have plagued entire familial lineages, HGE should not be shoved off the table. There should be certain cases that HGE is allowed and these cases should be strictly regulated. However, what diseases constitute this list of appropriate applications, how and for how long clinical trials should be conducted, and who makes such decisions are complex matters that must be discussed. Although differing cultural and social values differentiate nations' views on these issues, international consensus on, and legally binding agreements regarding these topics are imperative. These discussions must be informed by the public and by all stakeholders, particularly by those directly affected by the applications of HGE. Avenues to enable broad education of these and incoming proposals, the current state of the science, and risks and benefits of HGE will be crucial to our progress.

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Article

Palliative Sedation: Masked Euthanasia or Compassionate Care for the Dying?

Naomi DeTemple*

As a treatment tool in the care for the dying, palliative sedation is the reduction of a terminal patient's consciousness by sedative drugs to a level that relieves their refractory symptoms (Broeckaert and Nuñez Olarte 2002). Ethical concerns have been raised about the use of palliative sedation because of its perceived equivalence to euthanasia and incongruence with the goals of palliative care (ten Have and Welie 2014). Yet, if the criteria of proportionality, terminality, and refractory symptoms are followed and the intent of the physician is to minimize patient suffering while maximizing consciousness, palliative sedation is separate from euthanasia (ten Have and Welie 2014). Furthermore, if palliative sedation is responsibly used as part of a holistic and relational treatment trajectory, it can be a component of truly compassionate palliative care. Thus, palliative sedation is an ethically acceptable tool that can be used not to eliminate the suffering patient, but to value the patient as a person possessing worth and dignity.

Michael T. Wolf, a Certified Registered Nurse Anesthetist, related the following case study (Wolf 2013): "Jay" was a 33-year-old who received a diagnosis of advanced colon cancer. The next measures were "pain control and supportive measures knowing that his bowel obstruction would continue and symptoms might worsen." As Wolf cared for Jay, he built a relationship with him and his family, and they communicated about the kind of care Jay wanted and what pain control he could be given. He was able to receive care at home for a time, but eventually needed to be readmitted to the hospital. He "had become terminally ill, weighing little more than 45 kg (100 lb), with little desire for hydration or nutrition." At this point, changes were made in his care to manage his symptoms and pain, allowing him to have long periods of consciousness. "Jay's doses of medication were increased to hydromorphone, 4 mg/h, and lorazepam was converted to an intravenous infusion of midazolam (15 mg/h) for ease of titration." Eventually, Jay's pain could not be controlled with stronger medication. Deep palliative sedation was offered to create unconsciousness for pain relief and Jay consented to the propofol infusion. He was monitored as he rested comfortably with his symptoms under control until dying "peacefully with his wife and parents at his side."

Wolf's account describes a dying patient who received palliative sedation as an ethically acceptable component of his end of life care. The important aspect of Jay's case is that over time his care was adjusted to meet his changing needs, even as his symptoms later required palliative sedation. According to ten Have and Welie (2014), palliative sedation is defined by Broeckaert and Nuñez Olarte (2002) as:

> "the intentional administration of sedative drugs in dosages and combinations required to reduce the consciousness of a terminal patient as much as necessary to adequately relieve one or more refractory symptoms."

The question that arises regarding the use of palliative sedation is whether it is an ethically acceptable treatment separate from euthanasia and if so, if it is compatible with the goals of palliative care.

While it is a legal practice used in the United States, palliative sedation is an ethically debated treatment because of its proximity to the practice of euthanasia and potential incongruence with the goals of palliative care. Some authors point to the unclear or overly broad policy details, which could lead to palliative sedation becoming a type of euthanasia (Kingsbury 2001). Other authors raise concerns that palliative sedation decreases a patient's ability to communicate in relationships and could be used as a "quick fix" by physicians instead of meeting a patient's complex needs (Olsen, Swetz, and Mueller 2010). These concerns, according to ten Have and Welie (2014), could suggest that palliative sedation is contrary to palliative care's vision of relational and holistic care.

In view of all these concerns, palliative sedation may seem more like an ethical minefield to clinicians than a tool in compassionate care for the dying. Yet, palliative sedation is used in good conscience by some physicians. For example, Dr. Martha Twaddle, a Medical Director of Palliative Medicine & Supportive Care, values her patients as the multifaceted persons that they are and uses palliative sedation as part of her compassionate care for them (Twaddle 2019). Certainly the clinician's intent, as well as certain guidelines, should demarcate the ethical "safe-zone" within the broad practice of palliative sedation. Useful criteria, including proportionality, terminality, and refractory symptoms have been proposed by ten Have and Welie (2014). This paper expands on the proposition that palliative sedation is distinct from euthanasia when it is responsibly used with these criteria and the intent is to minimize the patient's symptoms while maximizing their consciousness. Furthermore, it proposes that palliative sedation is in agreement with the relational and holistic philosophy of palliative care.

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Background

Palliative Sedation

Palliative sedation was legally affirmed in 1997 with the two court cases Vacco v. Quill and Washington et al. v. Glucksberg et al. (Olsen, Swetz, and Mueller 2010; Vacco, Attorney General of New York v. Quill 1997; Washington et al. v. Glucksberg et al. 1997). Sedation can be administered with the informed consent of the patient or, if the patient is incompetent, the patient's surrogate decision makers. Concerning its efficacy, sedation at the end of life has been found to reduce refractory symptoms. Such symptoms, which cannot be controlled by any other interventions, can include "pain, dyspnea, persistent emesis, and agitated delirium" (Rousseau 1999, Braun 2000) which can stem from malignant tumors, congestive heart failure, neurological diseases, and chronic obstructive pulmonary disease (Cherny and Portenoy 1994; "Definition of Refractory Symptoms" 2013). Pertinent to ethical considerations, as more studies have been conducted to determine if palliative sedation causes or hastens the patient's death, it has been found that the administration of palliative sedation at the end of a patient's life does not hasten their death (Claessens et al. 2011; Maltoni et al. 2009; Morita et al. 2005; Stone et al. 1997; ten Have and Welie 2014).

Broeckaert and Nuñez Olarte's definition, which suggests that the purpose of palliative sedation is to relieve refractory symptoms, highlights what is considered ethical sedation by its narrowness. Sedation can be defined in different ways by those considering its use in end of life care. Sedation can also be called by different terms, including palliative sedation and terminal sedation. These terms can also be defined broadly. In general, palliative sedation specifies sedation that is administered for the relief of symptoms; on the other hand, terminal sedation tends to refer to both deep sedation, which is complete unconsciousness, or deep and continuous sedation, which puts the patient into complete unconsciousness at the start of treatment with the intent of keeping them in that state until death (Quill 2006; Rietjens et al. 2006; ten Have and Welie 2014).

Descriptors for duration (continuous/intermittent), reversibility, and level (mild/deep) are also included in or implied by the names of different types of sedation. The duration and reversibility of sedation are set by the physician either administering or withholding sedatives according to their intent (ten Have and Welie 2014). The level of sedation of a patient can be estimated with observational scales, such as the Richmond Agitation-Sedation scale ("Richmond Agitation–Sedation Scale" 2013); however, such scales may not accurately correspond to depth of sedation ("Medications of Choice" 2013).

The practice of sedation can also vary in the types of sedative medication used. Some physicians use benzodiazepines and barbiturates, while others use hanging drips with opioids, such as morphine. In other complicated cases, these medicines are used simultaneously (Billings and Block 1996; "Medications of Choice" 2013). Furthermore, guidelines placing limits on the use of sedation at the end of life are not necessarily consistent with each other (ten Have and Welie 2014). As expected from variation present in name, definition, descriptive qualities, sedatives, and guidelines used, sedation at the end of life is varied in practice. Upon examination, this wide field of sedation includes some practices that are ethically acceptable as well as others that are no more than masked euthanasia, certainly not ideal palliative care for the dying. The definition of palliative sedation must be narrowed if it is to be useful in determining the treatment's best use. As ten Have and Welie (2014) proposed,

> "rather than expanding the definition of palliative sedation to include practices that are intended to bring about the patients' death, it would make more logical sense to reserve the label "palliative sedation" for those sedative practices that are aimed only at symptom relief and apply the label "euthanasia" to all practices in which the patient's end of life is the principal aim or at least one of the aims of the physician's intervention."

Thus, palliative sedation can be differentiated from other practices that verge on euthanasia.

Euthanasia

In separating palliative sedation from euthanasia, it is important to explain why practicing euthanasia is clearly unethical. Euthanasia has been defined by one author as, "administering a lethal drug at the request of a patient with the explicit intention to hasten death" (Rietjens et al. 2006). This definition and discussion are limited to "active euthanasia," which is illegal in the United States and does not include those legal practices labeled as "passive euthanasia" like the refusal of life-sustaining treatment (Mitchell and Riley 2014; Pereira 2011). From a Judeo-Christian perspective, euthanasia is not ethical at a foundational level because helping a person take their life clearly breaks the fifth Biblical commandment, "'You shall not murder" (Exod. 20:13 New International Version; Rae and Cox 1999). God's command against taking innocent life only applies to euthanasia if one considers those at the end of life to possess personhood (Rae and Cox 1999).

It has been argued by proponents of physician-assisted suicide that a human being loses their personhood when their "biographical life", which points to an individual's expressed capacities, is lost (Rae and Cox 1999). This idea can easily be used to justify euthanasia, including the non-voluntary type, because a physician is not murdering a patient by taking their biological life when their biographical life,"the basis for personhood", is already gone (Rae and Cox 1999). Yet, a sound philosophical argument can be made that human beings, who are substances, derive their personhood not from their function, as this argument presupposes, but from their "internal essence" (Rae and Cox 1999). Substances, as opposed to property things, are ordered and functionally developed by their internal essence; they do not lose their identity throughout the process of change, as in a person's

development throughout their lifetime (Rae and Cox 1999). From the Judeo-Christian perspective, it is apparent that part of this internal essence constituting personhood is the image of God in each human being, for "God created mankind in his own image, in the image of God he created them; male and female he created them" (Gen. 1:27; Rae and Cox 1999). Because "a thing is what it is, not what it does[,]" the possession of personhood, and thus the right to life, is not

> "a bell curve, in which a human being moves toward full personhood in the first years of life, reaches full personhood at a given point, and then gradually loses personhood until the end of life[,]" (Rae and Cox 1999)

but rather a continuous line from conception to death that is set in permanent ink by the hand of God imparting His image (Rae and Cox 1999).

In addition to the substance view of a person and God's command not to murder, euthanasia is unethical because of mankind's relationship to God. Gilbert Meilaender takes a distinctive approach against physician assisted suicide and euthanasia by saying,

> "Within the story of my life I have the relative freedom of a creature, but it is not simply "my" life to do with as I please. I am able to end it, of course, but am not free to do so without risking something as important to my nature as freedom: namely, the sense of myself as one who always exists in relation to God" (Meilaender 2013).

Meilaender argues that human beings are in relation to God and under His authority, making it so that they are not free to end their own lives or the lives of others as they please (Meilaender 2013).

Meilaender (2013) also argues against euthanasia by affirming that, contrary to what its advocates contend, it is not compassionate care because compassionate care is not intended to "minimize suffering" but to "maximize care." Eliminating sufferers to minimize their suffering abandons them, but maximizing care "as they live out their own life's story" shows true compassion for them. This is in harmony with the long held Hippocratic medical ethical tradition of doing no harm to the patient. With the Hippocratic Oath, a physician swears that they will do "no harm or injustice to" their patients, and that they "will not give a lethal drug to anyone if [they are] asked, nor will [they] advise such a plan" ("Greek Medicine - The Hippocratic Oath" n.d.).

Palliative Care

Standing in stark contrast to euthanasia, palliative care is "person-centered care" and is the proper compassionate response of healthcare professionals to the needs of patients facing terminal illness (O'Brien 2014). Thus, palliative care should be the person-centered standard for palliative sedation. Palliative care, along with modern hospice, was brought about by the efforts of Cicely Saunders in the mid-twentieth century (Richmond 2005). Working from Saunders's concept of "total pain," which includes the physical, emotional, social, and spiritual dimensions of distress, palliative care seeks to provide holistic care for the patient (Richmond 2005; ten Have and Welie 2014; Twaddle 2019). A form of true care for the suffering, palliative care takes into account how the different expressions of the patient's personhood impact their suffering, which, in unison with a Judeo-Christian perspective, emphasizes the unity and importance of the inward and outward parts of a person (Cassel 1982; O'Brien 2014). With the ultimate goal of providing whole person care that considers not only the quality of life of the patient but the needs of the patient's family, palliative care follows Saunders' example of attentive listening and values the relationships involved in the patient's care (Richmond 2005; Rome et al. 2011). As Dr. Twaddle has described it, "Palliative care is about living well and landing softly— not the PAD [physician assisted dying] squad" (Twaddle 2019).

Proper care for the dying, palliative sedation is in harmony with a Judeo-Christian ethical perspective, demonstrated by Jesus' example of holistic care for the hemorrhaging woman in the biblical account (Mark 5:25-34) and by the parable of the Good Samaritan (Luke 10:25-37). In the account of the Good Samaritan, the word used for compassion denoted being moved to action (O'Brien 2014). Jesus' healing of the woman with the hemorrhage was not only physical, it was social and relational. Jesus "rescued her from a solitary life as a social outcast" by making her ritually clean (O'Brien 2014). In commenting on this same passage, John MacArthur proposes that the woman's healing was spiritual as well (MacArthur 1997). The holistic emphasis of palliative care echoes these examples of care for the whole person. Palliative care is compassionate care.

> "Compassion…is not reserved only for one's friends or fellow-believers, but is especially reserved for those who are marginalized, forgotten or abandoned in any way — whose suffering cries out for a response" (O'Brien 2014).

In this same sense, palliative sedation, when used with the same thought and purpose of palliative care, can also be considered ethical and compassionate whole-person care.

Criteria for Ethical Palliative Sedation

Criteria for use of palliative sedation give guidance to clinical practitioners for administering palliative sedation in a way that is both ethical and compassionate.

Intent

As proposed earlier, palliative sedation can only be considered ethically acceptable if it is separate from euthanasia. When examining the broad practice of end of life sedation, a key dividing line that separates masked euthanasia from ethical palliative sedation is the intent of the physician administering the sedative. The physician's intention is narrowly defined as "the plan or aim that guides the action," rather than "awareness and knowledge of foreseeable consequences of an action" (ten Have and

Welie 2014). In order for the sedation being practiced to be ethical, the intent of the physician must be to relieve the patient's symptoms while maximizing their consciousness. The intent cannot be to hasten or cause the death of the patient in ethical sedation. While it can be hard for physicians to determine, intent can be clarified enough to be used as a separating factor from euthanasia. This idea is affirmed by a study in which most euthanasia consultants interviewed thought " that the practice of CDS [continuous deep sedation] is clearly different from euthanasia because the intent of the intervention is different" (Buiting et al. 2011; Quill 1993; ten Have and Welie 2014).

Before the emergence of studies indicating that palliative sedation does not hasten death, the intent of the physician played an even greater role in the ethical validation of the practice. The principle of double effect, which hinges on intent, was frequently used to justify palliative sedation even if hastened death was a foreseeable outcome. The conditions for application of the principle are that the treatment is ethically good or neutral, the intent is for the good outcome rather than the bad outcome, the bad outcome is not the means for the good outcome, and the good outcome is greater than the bad. Yet, according to ten Have and Welie (2014), this principle became unnecessary for the defense of palliative sedation with the indication that " . . . palliative sedation has no impact on the length of life when the patient is already close to death . . . " (Noia 2017; ten Have and Welie 2014).

As will be shown with the proportionality criterion, the intent of the physician is demonstrated by how proportional the level of sedatives administered is to the severity of the patient's symptoms. Intent also determines the duration of the sedation. In order to avoid slipping into a masked form of euthanasia, the physician's intent must not be to sedate the patient deeply until death—proper intent to relieve symptoms requires that they only sedate the patient " . . . as much and as long as [is] necessary . . . " for symptom control (ten Have and Welie 2014). It is the intent to maintain the dosage of sedatives such that the patient is kept in deep sedation until death that renders some sedation irreversible,. This, however, immediately and permanently takes away the opportunity for the patient to revoke their consent for the treatment, much like euthanasia would, (Kingsbury 2001). It is also contended that irreversible sedation is unethical because the total unconsciousness it produces reduces the patient's life to "…a partially functioning, mindless human body[,]" which is "existential euthanasia" (Kingsbury 2001).

It is important to note that ethical sedation may end up being administered deeply and continuously until death, but only as is required by the patient's symptoms in the process of careful titration (ten Have and Welie 2014; Twycross 2019). This deep and continuous sedation is "… the outcome of a treatment trajectory; the need for it can rarely if ever be known in advance" (ten Have and Welie 2014). When deep and continuous sedation occurs in the process of careful titration, patients are given more of an opportunity to indicate how the sedation is affecting them or to revoke their consent during the titration. Furthermore, the loss of existential life is the unfavorable outcome, not the intent of the treatment.

Proportionality

Closely related to the issue of intent, the criterion of proportionality is a key divider between ethical palliative sedation and euthanasia. Proportionality means both that the benefits of sedation must outweigh the harm it brings and that "…the level of sedation applied…must be proportional to the severity of the symptoms" (ten Have and Welie 2014). According to some, palliative sedation is distinct from euthanasia because in palliative sedation the benefit of relief of symptoms can be greater than the harm of unconsciousness, while in euthanasia the relief of symptoms is not outweighed by the harm of death. Yet, it can be contended that the removal of the conscious work of dying—"…conscious decisions…[with] eternal consequences"—may be too great a harm to justify sedation (Shea 2004). Thus, the second meaning of the proportionality criterion holds more weight in making the distinction between palliative sedation and euthanasia.

As mentioned previously, proportionality acts as the indicator of intent. Ten Have and Welie (2014) affirmed that "the aim or intent is to relieve symptoms (and not to render the patient unconscious, let alone end the patient's life)…this intent…is evidenced by the manner of administration; specifically, the administration of the drugs is titrated according to the need to relieve symptoms (proportionality rule)."

In contrast, rapid administration of massive doses of medication or an increase in medication after symptom reduction has been achieved are indicative of the intent to bring about the patient's death (Billings and Block 1996; Kingsbury 2001; Quill and Lee 2000; ten Have and Welie 2014).

In speaking about her experiences with palliative sedation, one physician stated that she never renders people fully unconscious (J. Johnson phone communication 2019). She mentioned that it is common for those dying to have a sort of internal analgesia from toxins building up in their body and that on a scale of 0 (calm and alert) to -5 (not responding to painful stimuli) patients would only need to be sedated to -2 (tactile stimuli) in order to be comfortable. Keeping in mind that the more a patient is sedated, the less they are able to breathe, sedating a person beyond this point would be futile or probably hastening their demise. Thus, it can be seen that ethical palliative sedation includes administration of sedatives in proportion to the patient's symptoms, while the outlying practices of massive or increased sedative administration disregarding symptoms are no more than thinly veiled euthanasia.

Terminality

In addition to intent and proportionality, ethical palliative sedation is set apart from euthanasia by the criterion of terminality (ten Have and Welie 2014). A

common inclusion in various guidelines for the treatment, terminality refers to the requirement that palliative sedation only be administered to "…patients in the last stages of life" (ten Have and Welie 2014). Some point to the risks of death or the reduction or loss of consciousness as the basis for requiring terminality, which seems to imply that these risks are somehow less noteworthy for a patient nearing death. Yet, this is weak reasoning if one holds that the personhood, and thus the right to life, of a patient near death is just as present as that of a patient in any other stage of life.

A stronger argument for terminality lies in the fact that, while there are studies indicating that palliative sedation administered to patients close to death does not hasten death, sedation (especially complete) may hasten death when the patient is not in the active dying process and other palliative treatments are involved (Morita et al. 2005; Olsen, Swetz, and Mueller 2010; Smith 2009; ten Have and Welie 2014). Patients who are far from death should not be sedated because the treatment of their symptoms may require deep and continuous sedation, and if the patient refuses artificial nutrition and hydration (ANH), their demise could very well be brought about by starvation and dehydration (Ollove 2018).

ANH and palliative sedation are often discussed in relation to each other, but some consider them to be separate decisions (Olsen, Swetz, and Mueller 2010; ten Have and Welie 2014). Since ANH can be futile or have greater burdens than benefits and forgoing it during sedation does not hasten death for patients close to death, it is often forgone in deep and continuous sedation. Some arguments against the use of terminal sedation cite the withdrawal or withholding of ANH during deep and continuous sedation as the cause of death, making the sedation unethical (Battin 2008; Kingsbury 2001; Smith 2009). Yet, it can also be argued that if a patient is days or hours from death, ends up being deeply and continuously sedated, and refuses ANH, their death will not be hastened because they will have most likely already stopped eating and drinking (Olsen, Swetz, and Mueller 2010; Smith 2009; ten Have and Welie 2014). Sedated patients in the active phase of dying usually die of their underlying disease before they could die of dehydration (Smith 2009). While this argument shows that palliative sedation is ethical even without the administration of ANH, it becomes invalid with a patient far from death, making terminality a requirement for palliative sedation to be ethical.

Refractory Symptoms

Besides the criteria of intent, proportionality, and terminality, palliative sedation is ethically divided from euthanasia by the requirement of refractory symptoms for its administration. Cherny and Portenoy defined a refractory symptom as "'…one that cannot be adequately controlled despite aggressive efforts to identify a tolerable therapy that does not compromise consciousness" (Cherny and Portenoy 1994; "Definition of Refractory Symptoms" 2013). The criterion of refractory symptoms requires that further interventions be determined "incapable of providing adequate relief, …associated with excessive and intolerable acute or chronic morbidity, or…unlikely to provide relief within a tolerable time frame" before palliative sedation is used ("Definition of Refractory Symptoms" 2013). This ensures that palliative sedation is used only as a last resort and guards against its abuse for the purpose of avoiding costly and time intensive compassionate palliative care (Olsen, Swetz, and Mueller 2010; ten Have and Welie 2014). Refractory symptoms are how ethical palliative sedation is distinguished from sedation used merely because, "[i]t is far easier to increase the dose of midazolam than it is to wrestle with the underlying issues of a patient's care" (Roenn and Gunten 2009).

Other abuses, which blur the distinction between palliative sedation and euthanasia, can stem from the type of suffering that is qualified as refractory symptoms. While some consider psychological or existential (spiritual or emotional) suffering refractory symptoms, the criterion should be narrowed to require that physical refractory symptoms be the main motivators for the use of sedation (Kingsbury 2001; ten Have and Welie 2014; "The Problem of Psychological Suffering" 2013). It is true that "…non-physical suffering is legitimate and needs to be recognized, but[,]" as Olsen et al. noted, "this can pose a challenging therapeutic quandary given the difficulty in differentiating between appropriate responses to illness and psychopathologies such as depression" (Olsen, Swetz, and Mueller 2010). Additionally, concern has been raised over the disproportion between stopping psychological suffering and the harm of unconsciousness. Although requiring physical symptoms for sedation "…introduces a reductionist understanding of palliative care[,]" encourages the separation of body and mind, and thus may be contrary to the goals of palliative care according to some, the risk of the abuse of sedation were psychological suffering a valid determinant for it outweighs these concerns (Cassell and Rich 2010; ten Have and Welie 2014).

Congruence of Palliative Sedation with Palliative Care

The previous discussion has shown that when proper intent as well as the criteria of proportionality, terminality, and refractory symptoms are applied, palliative sedation can be distinguished from the unethical practice of euthanasia. Yet, in order for it to be an acceptable ethical practice, palliative sedation needs to not only be separate from euthanasia, but also fit into the vision of compassionate palliative care. In other words, ethical palliative sedation must value both the presence and multifaceted outworking of personhood in the dying patient. Concern has been raised that palliative sedation is in conflict with palliative care's goals of holistic and relational care for patients (ten Have and Welie 2014; Twycross 2019). Yet, these concerns have more to do with issues in current practice of sedation—the rise in use of continuous deep sedation and the "mission creep" of sedative practices that stem from the same convictions propelling euthanasia—than

with the way palliative sedation could be used by a concerned, compassionate healthcare provider. Like any tool in medicine, sedation can be abused, but it can also be used in a responsible, compassionate manner.

Relational

Ten Have and Welie worry that, "…palliative sedation brings us back to the days of old in which dying takes place in silence" and not toward relational palliative care (ten Have and Welie 2014). Yet, with the goal to take away as little of the patient's consciousness as possible, the ethical palliative sedation outlined previously should include few cases of deep and continuous sedation. While concern is warranted at the variation of practice from this expectation, "… the choice to sedate the patient may reflect the provider's behaviour or services' policy rather than the patients' preference or needs" (Peruselli et al. 1999; ten Have and Welie 2014). Continuous deep sedation, and thus dying in silence, could be minimized by the ethical convictions of the healthcare provider considering sedation.

Furthermore, definitions of palliative sedation imply that "… it is not an isolated intervention but a symptom control strategy within a palliative care trajectory…" (ten Have and Welie 2014). It can be inferred that palliative sedation can be in congruence with relational care if it is used as one tool out of many in a trajectory of whole person care. In this trajectory, titration can become a part of listening to and communicating with the patient, as the physician introduces sedatives little by little and converses with the patient or patient's family about the improvement of the patient's symptoms.

Holistic

The second concern with palliative sedation is that it "… suggests a return to medicine's traditional focus on the physical dimension of suffering and a physical response thereto…" (ten Have and Welie 2014; Twycross 2019). There is fear that palliative sedation is a "quick fix" that does not take into consideration the full range of a patient's suffering. However, this depends on how the individual physician uses it. While some physicians may replace true palliative care with a large dose of midazolam, use of palliative sedation does not require that it is the only treatment used. The physician utilizing it can recognize that there are many aspects to a person's suffering while affirming that it is important to minimize physical pain, which can affect the patient's quality of life and their total suffering (Cassel 1982; Katz 2002). As mentioned previously, ethical use of palliative sedation should result in the majority of patients retaining some level of consciousness. These patients may have improved social or psychological health as the removal of the distraction of distressing physical symptoms allows them to spend quality time with their loved ones (Twaddle 2019).

Pertinent to the discussion is the connection between physical pain and total suffering of the person. While it is affirmed that physical pain and total suffering are not the same, Eric Cassel notes in his article "The Nature of Suffering and the Goals of Medicine" that people with uncontrollable or overwhelming physical pain often report experiencing suffering (Cassel 1982). Overwhelming pain uncontrollable by any other means is a refractory symptom that palliative sedation could be used for and, if Cassel's observation holds true, this sedation may reduce the total suffering of the patient as holistic care should ("Definition of Refractory Symptoms" 2013; Seymour et al. 2015). Additionally, in cases when it is used intermittently or only once as respite sedation, palliative sedation may function simply to show the patient that their physical pain can be controlled. This could lead the patient to decide that they can go on without the intervention of sedation, similar to Cassel's example of terminal cancer patients whose suffering "…can often be relieved by demonstrating that their pain truly can be controlled…" (Cassel 1982; "Respite Sedation" 2013). Overall, from these observations it can be concluded that palliative sedation need not be in conflict with the holistic and relational vision of palliative care if it is used responsibly as part of a holistic treatment trajectory.

Conclusion

Returning to the opening case study (Wolf 2013), Jay's story illustrates the type of ethical palliative sedation a clinician could give their patient in good conscience. Sedatives were given, not to put Jay into complete unconsciousness from the beginning, but in proportion to the symptoms he experienced. From Wolf's actions, it is apparent that his intent was to control Jay's symptoms while affording him precious "long periods of consciousness." Jay was deeply and continuously sedated for two days before his death, but this was only after all other options were exhausted, including lesser levels of sedation. Furthermore, because Jay was terminally ill, already had "…little desire for hydration or nutrition,", and was near death when this occurred, his demise most likely was not hastened by starvation or dehydration during the deep and continuous sedation.

Throughout the account, Wolf took the time to give Jay the care that was best for him and did not abuse sedation in order to save time or money, evidenced in part by his use of sedation only when Jay's symptoms were refractory. Because Wolf followed these criteria of proportionality, terminality, and refractory symptoms, it was clear that he was giving Jay ethical palliative sedation, not thinly guised euthanasia. Additionally, though Jay's case required more care than hospice could provide, Wolf carried out the vision of palliative care by building relationships, communicating well, listening to what Jay and his family wanted, and prioritizing Jay's time with his family as much as possible. While some condemn palliative sedation as a form of euthanasia, Jay's story demonstrates that with the proper criteria and intent, palliative sedation can be ethically acceptable, compassionate care for the dying that values the patient as a multifaceted person and a fellow human being, who has value, dignity, and worth.

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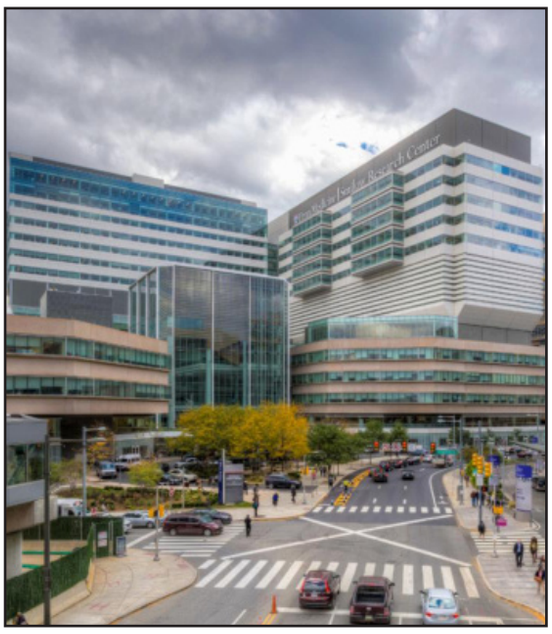

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