

Correspondence

Like/As: Metaphor and Meaning in Bioethics Narrative

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We would like to thank Cynthia Cohen for her critique of the report of the first stages of the NIH Roadmap Grant on Oncofertility, which is just in the first years of the animal modeling phase, although the research is continuing to unfold beyond the stage at which this first article, which sought to lay out the critical questions in the field, was written. Cohen has long been attentive to the risks involved in the manipulation of human reproduction and the cost that is borne by society for scientific innovation. Despite our respect for her considerations, and for the body of her work, we think that, in balance, her reading of the article in question is wrong on several counts. It is important to re-emphasize the very early stage of the described research, for while we would hope that medical research leads to effective responses to human suffering, we make no claims that this research will prove as effective in women as it has in female mice. We thus find it ironic that Cohen, who is concerned that we might be overly enthusiastic, is herself largely concerned with events that would only occur decades in the future, if they occur at all. In fact, the problem we currently face is that we do not know—and *cannot* know—whether the research will yield therapeutic results. This is defining the ethical question: What is the right thing to do in a situation of complete uncertainty, in which the therapeutic use of this research will be found—if one is found—long after the childhoods of the children involved have ended?

We responded to this question with recourse to a narrative which justified a next step of empirical research. To answer our question, we believe it is important to draw upon the reflections of actual women who truly stand to be impacted by this research. This empirical research is born from our feminist conviction that asking the actual women who are the subjects of the gaze tells us what is important to them and informs us of the perspectives of those who must

live at the center of the story we tell. Accordingly, we asked the women best able to reflect on the matter—childhood cancer survivors, now grown and in remission—to tell us their thoughts about the uncertainty involved in oncofertility research.

We framed our understanding of the issues using a metaphor from Genesis rather than standard “bioethics principles” because the language of principles is but one way of describing what is at stake. Literature, scriptural texts, and personal narratives also offer rich resources for framing ethical discussions and, by extension, determining which principles are most relevant to the case at hand.

The biblical story of Joseph captures the spirit of oncofertility research in the following way: faced with foreseeable but not certain loss of fertility (either the land’s, in the story of Joseph, or a woman’s, in the case of cancer,) how can societies or persons best prepare? The issue of trying to prepare against such loss, even if the evidence for its urgency is based on dreams (in the case of Joseph) or hypothesis (in the case of science) is not limited to this research. Knowing that we cannot know should be a core premise of all translational research, despite our commitment to act as well as we can. Is it worthwhile to take steps to protect against the impact of this loss (by storing either grain or ovarian tissue), even if the success of these preemptive steps is uncertain?

Cohen appears to have misunderstood the use of the Joseph motif, suggesting that the offered analogy equates the values of survival and fertility—that somehow oncofertility researchers (many of whom are oncologists), have lost sight of the fact that surviving cancer must be the most important goal of cancer treatment. Yet just as it would not have made sense for the Egyptians to store grain for the future famine if doing so would have caused people to starve during the years of plenty, it does not make sense to attempt

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to preserve a woman's fertility at the expense of her life, a point that is clearly understood by every researcher, physician and bioethicist involved with this project.

Furthermore, the primary purpose for using the Joseph story is to talk about dreaming and Joseph as the dreamer against all odds. Cohen worries that this makes us enthusiasts, and that this enthusiasm taints our capacity for sober discernment of ethical concerns. Yet the Joseph motif serves as an important reminder that this research *is* grounded on what scientists still only *hope* they may be able to accomplish. Our research on ethical questions raised by the uncertainties of this technology is understood to be a core component of the larger oncofertility project, as is the research of the social scientists, legal theorists, and policy analysts that are all contributing to this interdisciplinary work.

Here, we ask a basic question: Can bioethicists be optimists? Must we only portray scientists as corrupt, fallen, tempted beings, "pimps for the drug companies," as Carl Elliott suggests? If we respect the work or the moral gesture, does it mean we have had one put over on us? Does our respect for scientists who actually take seriously our admonitions about needing to shape research toward human suffering seriously imply a lack of rigor?

We argue that it does not. Medical research is a genuine moral gesture. It can be corrupted, as can any moral gesture. Moral agents can fail, and this failure can lead to harm, as can any failure of judgment—including those committed by bioethicists, whose power to stop research, stop trials, and stop funding is as profound a power as any. At times, we, too have failed, as a field and as individuals, but our failure to enact our role-specific duty does not render the entire project of bioethics suspect. It is true that we *are* in favor of research and treatment that relieves human suffering, and frankly, we *do* hope it succeeds; that is why we attended to this project in the first place.

Ethics needs a hermeneutics of suspicion, to be sure, but a hermeneutics of reactive opposition is an error. "For what should I hope?" asks Immanuel Kant, reflecting on the meaning of living a fully human life. Seeking better ways to facilitate a full recovery from cancer is surely a telos we should all hope for.

In her article, Cohen then raises the issue of cancer transmissibility. We find that this may be a serious error as well. We suspect that she is considering the ethical choices of a woman with, for example, BRCA1 using the technique. We find this troubling: for *if* we believed that women (or men) with oncogenes should not have children who risk bearing the same genetic marker as their parent, then we should make the same critique of women and men who conceive naturally or use conventional IVF after they recover—and of course, we do not, nor should we. Why then is it suddenly an unacceptable risk for only women with the most iatrogenic harm to have children, and to use this form of ART, should it become possible to do so? Cohen is right to point out that for women whose cancer is genetically-based, in vitro follicle maturation does not eliminate the risk of transmitting cancer-related genes to children—but this is neither

a reason to not become pregnant and bear such children, nor is it a reason to abandon research on follicle maturation altogether. Rather, it is a factor to bear in mind when determining who should participate in this study and, should this technique prove successful, who should consider utilizing this technology, and with what advice.

We are similarly puzzled by Cohen's reflections about the proposed pediatric aspects of the study. She suggests an elaborate clinical trial. It is not clear who the "matched control children" are that Cohen insists upon including in the study. Is she proposing that sections of "ovarian" tissue be removed from young girls who do not have cancer? Doing so would be even more ethically troubling than removing sections of "ovarian" tissue from young girls about to undergo cancer treatment that will likely diminish their fertility. Is she proposing that some young girls with cancer *not* have an ovary removed as part of the study? How exactly would children in the control group differ from children not participating in the research at all? While we deeply respect the model of anonymized (aka double-blind) placebo-controlled clinical trials, it is difficult to imagine how to construct such a trial, since the intervention is a) not intended to be directed toward the body of the patient, but toward the removed tissue itself, and b) since the final proposed phase of the trial may take place decades later. It would be difficult; if not impossible; to defend a placebo trial in the study of treatments for infertility.

Cohen is also concerned by what we call "the Avatar Problem," in which a bioethicist imagines a bitter, unhappy future teen who is trapped by the choices made by her parents on her behalf, parents that she is suspicious of, and does not trust. This avatar's imagined critique then becomes a justification for halting the proposed technology. In general, we believe that the bitter avatar argument is flawed for many reasons. Its use is *particularly* odd in this case, since our research has sought to engage the very demographic she fears will regret such an intervention: teen and adult cancer survivors. Let us repeat: *it is this community of women, many of whom point out that young men have long been able to cryopreserve their sperm (despite similar issues with the hereditary nature of some cancers), who have called for this research to proceed.* We consider the opinions of the actual, particular patient far more important than the hypothesized opinions of imaginary patients occupying an imagined future. This practice follows the long-standing regard our field has demonstrated for other patient advocate communities, such as persons with AIDS or the disabled, in voicing their concerns and becoming involved, as is this community, in research design and telos.

Cohen, like so many bioethicists this year, does seem enthusiastic about one basic research project, despite the fact that it has only been published in four papers that describe the mouse model: induced pluripotent stem cells (iPS cells). While the use of iPS cells to create gametes might, if successful, render Oncofertility research on follicle development irrelevant, it is not entirely clear that this is necessarily the case, nor does iPS cells address Cohen's concern about

genetic transmissibility. Even if there could be certainty that iPS cells are physiologically identical to hES cells, the question of whether they could be coaxed into human gametes at all would only be the beginning of their use. It may be difficult to construct a safe and ethical experiment in humans to know that these “derived, and then re-differentiated,” oocytes could be used for actual human reproduction. For the time being, at least, research in iPS cell technology is not a reason to abandon the project of researching follicle development as a method of fertility preservation. Even if iPS cells *could* be regularly reprogrammed to develop into gametes, it is not clear that the use of iPS cells, while less invasive, would be any safer, or any less cost-prohibitive, than follicle maturation and cryopreservation.

Cohen turns her attention to a series of rules that might guide the basic science as it moves toward human use. We agree and have set similar guidelines. Our initial article was not intended to describe such structures; indeed, the entire project is under a multiyear consideration by an external bioethics advisory board of leading scholars who will address these questions. This article was intended to define the terms and the success in animal trials and engage a wider circle of scholars in reflection on a new direction in human reproduction. As the work goes forward, our group intends to reflect on the issues that emerge in cases and at benchside consultations. While the ground covered by Cohen has already largely become part of all trials, we contend that new problems remain to be considered when women simultaneously hold the roles of patients, tissue donors, and perhaps, experimental subjects. There is a long path ahead to move from animal models to human therapies, but in this regard too, oncofertility is similar to any other medical research hypothesis—it is scientific research and not a faith claim precisely because it can be falsified, and may indeed prove to be impossible. The various questions Cohen raises are surely not reasons to halt “oncofertility research”—they are part of the many questions that the researchers intend to explore with the ultimate goal of delivering answers.

We wish to correct a final misreading, and to clarify the title of the original paper, “Waiting to Be Born.” The paper is the subject of a longer work by one of the authors (Zoloth). Though it does imply, which was NOT our intent, “images of possible children waiting in an alternative universe hoping to escape to this one,” (Cohen 2). The purpose of the particular terminology chosen for the title was to highlight the play on words. The technology is waiting to be born, and the ironic literary illusion to William Butler Yeats’ poem. “The Second Coming” is intended to note our essential position that the future is uncertain, and that we are fully aware of our duty to be alert to what is waiting to be known, and thus in this sense “born” and borne. The reference to the Yeats poem is like the complex metaphor behind the use of the Joseph text in Hebrew Scripture, in which

the dreamer policy-maker Joseph cannot know anything for certain: whether his fears that barrenness may overtake the land, or whether his idea for the storage of grain, which requires the cooperation of an entire society can even be technically accomplished, or how his own family will be affected. He only knows that the vulnerable will need a new chance, and that to not even try will surely end in sorrow. But the story is deliberately multivalent: Joseph sets up the centralized administration and forced taxation of the very state that will come to oppress the Hebrews and enslave them; he will save a society that will stand by when Hebrew babies are killed—one cannot know the future. While we are indeed hopeful that women and girls who survive early onset of cancer will be given the same choices that men have, and indeed will not need immediate hormone regimens, “emergency IVF,” and the abrupt creation of embryos, a careful reading reveals that our chosen narrative conveys our concerns as well. Yeats calls his poem “The Second Coming,” and our glancing use of the reference was meant to convey and carry the complexities of our task. We reprint it in its entirety here:

The Second Coming

Turning and turning in the widening gyre
The falcon cannot hear the falconer;
Things fall apart; the center cannot hold;
Mere anarchy is loosed upon the world,
The blood-dimmed tide is loosed, and everywhere
The ceremony of innocence is drowned;
The best lack all conviction, while the worst
Are full of passionate intensity.
Surely some revelation is at hand;
Surely the Second Coming is at hand.
The Second Coming! Hardly are those words out
When a vast image out of *Spiritus Mundi*
Troubles my sight: somewhere in sands of the desert
A shape with lion body and the head of a man,
A gaze blank and pitiless as the sun,
Is moving its slow thighs, while all about it
Reel shadows of the indignant desert birds.
The darkness drops again; but now I know
That twenty centuries of stony sleep
Were vexed to nightmare by a rocking cradle,
And what rough beast, its hour come round at last,
Slouches towards Bethlehem to be born?

REFERENCE

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