INTRODUCTION

Rates of end-stage organ failure continue to increase globally, and organ donation rates have not kept pace. At the same time, scientific knowledge about, and experience with, xenotransplantation (XTx) continues to advance, foreshadowing the possibility the immunological, physiological and safety-related barriers to the clinical adoption of XTx as a therapeutic option may soon be traversed, which raises many challenging ethical and social issues for consideration.

The theological-ethical perspectives and the complex issues that XTx raises for society and the potential recipient have been widely reported. Public opinion surveys have found that, in general, the perception of and willingness to consider XTx are favourable, although the influence of religious beliefs was less straightforward. While theological discussions have suggested no specific prohibition from Abrahamic theological traditions (ie Jewish, Christian, and Muslim), a review of public opinion survey responses related to the role of religious beliefs in the decision to consider a XTx was more complex. One recent study suggested that it was the amount of detailed information and procedure results that would have the greatest influence on religious acceptance of the procedure.

Given the reality of future clinical trials, it is important to explore how various religious traditions might view XTx as a therapy, to better understand their theological views how each might address the importance of human health, and the use of pigs to bring health to others. A full understanding of the beliefs and practices of the Jewish, Christian and Muslim traditions will be necessary to fully prepare for, and implement, clinical trials of XTx.

The following information does not suggest that these are the only religious views that need to be explored or considered, nor is it the final word about Abrahamic interpretations. Rather, the
following is a foundational exploration of the opinions from three major theological traditions. It is hoped that this material will serve as a source for future discussions among XTx programmes to help promote theological understanding and respect for the influence that they may have on the individual patient. A necessary component if XTx is to achieve full public acceptance and support, while recognizing that, for some, the decision to seriously consider a porcine organ transplant may never be possible because of their individual religious beliefs.

2 | JEWISH PERSPECTIVE

The issue of XTx from a Jewish bioethical perspective is a matter of halakhah, Jewish law. Halakhah has its origins in the Torah, the first five books of the Bible, continuing over the millennia with rabbinic writing from the ancient Midrash and Talmud, through mediaeval and modern law codes and responsa literature (letter decisions, including compilations). Traditionally, such works were accessible only to adepts (ie experts) and scholars. Today, the depth and breadth of Jewish law generally, and of bioethics specifically, are more readily accessible through academic and topical publications.

2.1 | Issues of Halakhah (Jewish Law)

Regarding XTx, the halakhic issues seem to involve at least these: the duty to heal, the obligation to save human life, the prohibition on cruelty to animals, the dietary laws and forbidden mixtures.

2.2 | Duty to heal

The duty to heal human life in Judaism has been derived from various scriptural references. Both great mediaeval rabbinic authorities, Moses Maimonides and Yosef Karo, identified this duty in their writings. “The Torah gives permission to the physician to heal; moreover, this is a religious obligation and it is included in the obligation of saving a life. If he withholds his services, he is considered a shedder of blood....”

It is a religious duty, that is to say, a physician is obligated by law to heal the sick.... This is included in what [the Sages] said in explanation of the verse, “And you shall restore it to him” (Deut. 22:2)—to include his body, that if he saw him lost and he can save him, he must save him with his body or with his money or with his knowledge....

The duty to heal and seek medical care is not absolute, as Jews readily embrace human life as mortal. Jewish law does, at times, permit physicians to provide risky or experimental treatments and procedures, and patients to accept them. The specific circumstances of any given situation will govern whether such medical interventions are required to be tendered or mandatory to be received. Also, medical care that is futile or unhelpful may not necessarily need to be given or accepted, especially towards the end of life.

2.3 | The obligation to save human life

Two of the most critical words found in the Torah translate into, “so choose life.” From this and other Torah teachings, the ancient rabbi derived a point of halakhah that is now deeply ingrained into the Jewish soul: the obligation to save human life, pikuach nefesh. According to the Talmud Sanhedrin 74a-b, saving human life is a paramount value in Judaism. It is so important that it takes precedence over all other Jewish values. Even the laws of the Sabbath and Holy Days are suspended to save life. The obligation to save human life is superseded only by the prohibitions to commit idolatry, murder and sexual misconduct.

2.4 | Cruelty to animals

People are stewards with dominion over earthly creation. This is a unique responsibility with humans having so much power to control the fate of fauna (and flora, and even over each other). While people can use animals and other sentient creatures for work, food and pleasure, causing pain and suffering should be avoided.

“If you see the ass of your enemy straining under his load, and you refrain from unloading it, go and unload with him” (Exodus 23:5). This verse is one of the main sources for the prohibition of causing unnecessary suffering to animals (Talmud Bava Metzia 32b). While man was given dominion over the animals (Genesis 1:26), this dominion is not one of tyranny, and it has limits. Any time we use animals for our benefit, we have to be sensitive to their feelings and avoid any unnecessary pain.

It is clear that turning to animals as donors for human medical care necessitates experimentation, procedures, genetic modification and other things that might be deleterious and distressful to the animals. To the extent that xenograft technology can help save human life, the use of animals in this venture is acceptable under Jewish law.

In the 20th century, rabbinic opinions have generally permitted animal experimentation for medical research and the use of animals to save lives.... [T]he Jewish religious tradition... forbids any act which causes pain or discomfort to an animal unless that act satisfies a legitimate human need.... [E]very effort must be made to eliminate or minimize the pain that might be experienced by these animals.

2.5 | Jewish dietary laws

Observing the laws of kashrut, keeping kosher is a traditional Jewish spiritual practice. This is not the place to weigh into the specifics
as kashrut is both detailed and nuanced. Books on the subject are popular and varied.\textsuperscript{30, 31} Suffice it to say here that employment of non-kosher animals as xenograft sources in health care can be seen and felt as problematic.

Nonetheless, the Jewish dietary laws can also be overridden to save human life. It has long been held that one must accept medication containing non-kosher ingredients to counter a life-threatening illness.\textsuperscript{32, 33} The Jewish response to XTx using non-kosher animals, such as pigs or baboons, is to similar effect.

People who observe the Jewish dietary laws are forbidden to raise pigs or eat their meat.\textsuperscript{34} Although Judaism prohibits the consumption of pork, it does not forbid deriving benefit from pork. Thus, for decades, the use by diabetics of insulin made from pork has been permissible in Jewish law, as is the use of porcine heart valves.\textsuperscript{29}

2.6 Forbidden mixtures

The halakhah of kilayim, forbidden mixtures, is a complicated subject in and of itself. Traditionally, this concerned mixtures of crops, animals or clothing materials. For present purposes, the problem is one of animals, both with respect to xenografting as a concept and genetic modifications to the donor animals (or perhaps recipient humans) as a technique.

The mediaeval scholar and mystic Moses Nachmanides provides us with a succinct objection the comingling of animals: “One who grafts together two species alters and undermines the work of creation. It is as if he thinks that the Holy Blessed One did not complete the needs of His world, and he desires to assist in His creation of the world by adding more creatures to it.”\textsuperscript{34}

The halakhic prohibition seems to address sexual unions and the genesis of artificially new species. XTx, as we are conceiving it today, does not involve either. “…[T]he mixture in this transplant not being a sexual mating but a mere physical juxtaposition, it constitutes no objection in the case of necessary healing.”\textsuperscript{35}

There is no reason to be concerned about implanting the heart of a … beast in a human being. For we are convinced that the transplanted heart … will be nothing more than a pump for the provision of oxygenated blood to the brain, with no influence whatsoever on the human, intellectually or psychologically. … [T]here will be no changed identity of the person… [T]here should be no halakhic or Jewish ethical reservation regarding the transplantation of a heart of an animal … into the chest of a human being.\textsuperscript{36}

Genetic modifications are to similar effect, at least currently. The Jewish community from Reform to Orthodox views genetic engineering and gene therapy as appropriate medical means and methods to prevent, treat and cure disease, not transgressing the laws of forbidden mixtures.\textsuperscript{37}

Most modern methods of genetic engineering are not directly compatible to the actions forbidden as [mixtures] by the Bible or the rabbinic literature, since recombinant DNA generally includes just snippets of foreign genomes that function as widgets in their recipient…. [T]he motivation to save human lives and enhance therapies that use genetic engineering … would suffice to permit that which might otherwise be forbidden…. The Torah’s ban on [kilayim], the physical blending of different species of plants or animals, does not extend formally to the modification of gene sequences via the introduction of foreign DNA in order to convey a specific capability in the new organism…. The creation of dual species human/animal chimera is forbidden. Modifications of the human genome intended to combat illness are permitted, for they may promote human health and protect human dignity.\textsuperscript{38}

3 CHRISTIAN PERSPECTIVE

Any Christian reflection and analysis of the possible use of XTx in human beings will be grounded in the fundamental call all Christians have received to follow the example of Jesus Christ in reaching out to those in need to bring healing and comfort. As Jesus has done for us, in bringing healing to all of humankind, particularly in restoring our relationship with God, which had been damaged by human sinfulness, so, too, we are called to heal others who experience a separation from the human community due to illness of any kind—physical, mental, social or spiritual.\textsuperscript{39} Hence, when we examine the potential use of XTx as a medical treatment, we must always look to its effects on the entirety of any person to be treated in this way.

3.1 Treat the whole person

This need to look at the whole person comes from the fact that the many miraculous healings that Jesus performed had both physiological and relational aspects to them. The people healed experienced both a relief from their physical or mental suffering and a reconnection with their loved ones or community—a relationship the illness had damaged or severed. Therefore, the ultimate goal of our caring for those in need is to foster and enhance the loving relationships we are called to have with each other and with God. Mere physical or mental repair is never sufficient and should be undertaken as a means towards the restoration of the patient’s relationships with family and friends. This perspective means that even when no physical or mental repair is possible, we can always intercede to give care to a patient that will help respect and foster the patient’s loving relationships—including unto death.
3.2 | Appropriate use of animals

From this relational perspective comes a second Christian concern regarding XTx: the appropriate use of animals in human research and treatment. Although the Christian tradition emphasizes the important place human beings have in Creation—as the creatures made in the image and likeness of God—this exalted position carries with it the responsibility of caring also for the rest of Creation as we strive to care for other human beings. Hence, while we have been given the power and ability to use other creatures in Creation to achieve human goals, such as healing people, we must always use those powers and abilities judiciously and with respect for the amazing gift of Creation, including animals that we have received from God.

3.3 | Treatment impact

The third relational aspect that must be considered regarding any medical treatment to be developed is the impact a given treatment will have on the human community in its entirety. This concern includes the number of those in need who will have access to the treatment, the possibility that pursuing a XTx option may syphon resources away from others who are also in need of medical care, and any other detrimental effects a treatment such as XTx may have on the human community in general—such as the consequences crossing species boundaries could have on human identity and sacredness.

3.4 | Relational emphasis

Using these three key relational emphases of the Christian Tradition, a relatively clear response can be given to the issues raised by XTx. First, as for all medical treatments, one can do a risk/benefit analysis for any given XTx treatment. If the risks to a patient’s health (physical, mental, social and spiritual) do not outweigh the realistically anticipated benefits (individual, familial and communal), then the procedure can be legitimately pursued if freely chosen by the patient, or the patient’s designated surrogate. Of course, many of the issues (ie social and communal) will have to be addressed during the development of any treatment, such as the risk of exposing the human community to animal diseases, and the scalability of the treatment for all who may need it. The importance of these issues has already significantly influenced the development of the XTx field. Another issue that will certainly be decided on a social level will be the decision to exclude certain organs and tissues from the list of appropriate organs and tissues to transplant. Brain and reproductive organ transplantation are two examples of organs and tissues that would not be available for transplantation from a Christian perspective due to the momentous personal and species identity issues that would arise from such procedures.

As mentioned above, animal safety, as well as human safety, will also need to be addressed. Although the Christian Tradition certainly allows, and even encourages to some extent, the use of animals to promote human flourishing, animal use must be done with due attention given to the avoidance of abuse or misuse. This issue will be critical when assessing the stress and pain the animals undergo in the process of making them amenable to organ transplantation for humans, and when calculating the number of animals that may be required to meet the needs of patients requiring transplantation. One potential solution to these issues would be to clarify that only a subset of all transplant patients would be best served by XTx, while most others may be best served by other treatment approaches that do not involve the use of animals. Hence, the justification for using animals in this way would be that a limited number of animals are needed as organ donors as they are the only viable option for a certain subset of patients in need of organs.

4 | ISLAMIC PERSPECTIVE

The ethical dimensions of XTx from an Islamic perspective require the consideration of several caveats. First, like many religious traditions, the Islamic tradition is plural, and multiple perspectives can be found on just about any issue. The second issue is that there are many different moral sciences within the Islamic tradition, and each of these provides insight into the “ethical.”40-42 For the purposes of this paper, it should suffice to note that the commentary will draw upon the Sunni moral theology,42 and primarily focuses on Islamic legal perspectives. While the Sunni or Shia views might have a slightly different approach to deriving moral law from the scriptural sources, none ignore scripture; Islamic law is normative and involves scriptural reasoning. Therefore, the questions to be addressed are the following: Would XTx be judged to be permissible according to Islamic law? What are the principal ethico-legal constructs and issues that inform such an assessment?

To discern Islamic ethico-legal perspectives on XTx, we need to consider the moral status of the act along with its intended aim, the implications of the act upon the agent and the acted upon, and the societal considerations involved with the practice.

4.1 | Ethico-legal considerations based on the end-goal of XTx

Xenotransplantation is viewed as a potential medical therapy for individuals who suffer from heart, kidney, pancreas and potentially lung and liver failure. Current research studies the uptake of xenografts which involve whole organ transfer, for example heart, as well the transplantation of tissue and cells, for example insulin-producing pancreatic cells, from pigs to humans.2,44 As XTx is a potential medical therapy it is important to recognize that, in general, Sunni Islamic law judges the seeking of medical treatment as permissible but non-obligatory.45,46 According to the majority view, seeking clinical treatment becomes ethically mandatory when the proposed therapy is certainly life-saving, in other words, it assuredly will save a patient’s life.47 The scientific evidence for XTx does not yet support the claim that the treatment is life-saving because xenografts have limited survival and even life-saving xenografted hearts have only sustained function for months.48 Such limited longevity detracts from claiming
it is a curative, life-saving procedure, and at present it might at best simply be a stop-gap intervention. With respect to XTx as a cure for kidney, liver and pancreatic failure, there are other potential therapies for kidney failure, that is, dialysis, and similar issues with xenograft failure rates are found. Thus, from an Islamic legal perspective XTx might, at best, be considered a permitted therapy but not one that is morally obligated for patients to seek. At the same time, should the harms of therapy outweigh posited benefits, the legal assessment could change to reprehensible or forbidden status. In the light of these considerations, multiple Islamic jurists have deemed XTx as legally permissible, with several contingencies (to be discussed below).

4.2 Ethico-legal considerations based on the source of XTx

The legal permissibility is conditional and rests on several issues. For one, some scholars argue for permissibility on the basis of the concept of ḍarūrah or dire necessity. The ethico-legal concept of ḍarūrah is invoked to overturn a normatively prohibition when a life threat or similar hardship exists, there is no alternative solution, and the proposed solution does not directly entail harms that outweigh the benefit. In the case of XTx, some jurists restrict their permissibility to cases where a non-porcine animal is used. Others invoke ḍarūrah as the basis for permitting porcine-based XTx. This contention is based on the fact that the pig is considered to be najas al-`ayn, or intrinsically impure, according to majority of Sunni scholars. Therefore, any part of it—be it skin, bones or organs—cannot be used by Muslims for medical purposes. Some jurists permit porcine products to be used on the basis of ḍarūrah, or when the pig undergoes essential transformation, istihāla, such that it is no longer deemed to be pig, but a wholly new substance. It is important to note that some scholars resist these arguments and argue that ḍarūrah cannot be invoked because the Prophet Muhammed is reported to have stated that cures are not to be found in impermissible substances. Also important is to understand that the istihāla construct is defined differently by different schools of law, and the evidence for istihāla having occurred is ill-defined. Nonetheless, it would appear that istihāla does not apply to XTx because the genetic alteration of pig DNA is relatively minor in XTx, and thus its origin and essence remain.

These issues are lessened when other animals, for example baboons, serve as the sources of XTx. For one, other animals are not considered intrinsically impure although their organs or tissues might still be considered juridically impure and thus only used when there is no alternative. Issues of animal welfare and their instrumental use also need to be considered when outlining an Islamic bioethical position. The Qur’an refers to the human being as God’s honoured creation (17:70), humankind’s vicegerency (archaic English term for stewardly responsibility whilst standing in for God) (38:26) and that the rest of creation has been put into humanity’s service (14:32-33 and 45:12-13). At the same time, Islamic scriptures also remind humankind that they will be called into account for the way in which God’s bounties are put to use and that this stewardship responsibility is a grave burden (33:72). Consequently, while using animals to promote human well-being is perfectly acceptable, they must be treated with due respect as God’s creation and be well-treated. Indeed, Islamic rules of slaughter reflect these notions, for God’s name must be invoked prior to striking the killing blow, and the animal must be slaughtered in a way so as to minimize pain by slitting of two of the three “pipes”, the jugular vein, carotid and trachea, in one blow. Indeed the Prophet Muhammed stated when referring to the practice of slaughter that, when one proceeds, he should do so recognizing that God is watching and that he must adopt excellent form when doing so. Muslim farming practices and dietary laws aspire to upholding these ideals.

Harkening back to the issue of XTx, Islamic bioethical ideals would not necessarily reject the purposeful usage of animals but might find the way in which animals are reared for XTx to be problematic. Specifically breeding animals with a weakened immune system, rearing them in pathogen-free conditions that deprive them of natural habitats and foods or other similar “farming” methods might find objection from Islamic scholars. Similar reasons lead some Islamic legists to find fault with animal experimentation in medical research. As XTx moves from being a topic of research to representing a conventional therapeutic modality, Islamic scholars will need to work out guidelines for animal welfare and treatment as related to XTx.

4.3 Ethico-legal considerations with respect to the recipient of XTx

From an Islamic perspective, the principal consideration for recipients is adequate knowledge to make an informed decision. Humans are moral agents, and every decision we undertake is of moral significance. In the realm of medical research and health care, Islamic scholars assess the moral significance of a patient’s therapeutic decision based on a careful weighing of harms and benefits. In general, the removal of harms takes precedence over bringing benefit (dar’ al-mafāsid `awla/muqaddam min jaib al-maṣālih), thus harms of potential treatments must be carefully enumerated and considered.

The field of XTx presently struggles with estimating the harms of the potential therapy. For example, there is a risk that a transplanted organ might carry viruses or other pathogenic substances that can harm the recipient. Other health risks include the known increased risk of diseases incurred as a result of taking lifelong immunosuppressive medication. Similarly, depending on whether organs, tissues or cells are involved in XTx, there are a host of risks related to graft vs. host diseases and organ rejection.

4.4 Ethico-legal considerations at the level of society

Islamic ethico-legal assessments take into account individual and societal implications of actions and mediate between concerns at each of these levels. Several societal considerations deserve attention
from an Islamic lens. One issue revolves around equity; would XTx be a therapy restricted to the wealthy or would it be offered to all-comers? Islamic moral visions of healthcare provisions stress social justice and equity, and Islamic scholars tend to recoil at systems of care that are discriminatory or otherwise non-universal. While concerns of equity are not unique to XTx, the potential high costs associated with the therapy and the present non-equitable structure of health care ordering in the United States would give pause to ascribing unconditional Islamic sanction to the practice.

5 | CONCLUSIONS

The consideration of theological beliefs presents XTx programmes with serious and complex views to consider. As evidenced by the existing literature, theologian opinions are not always consistent with those of potential patients. The current work illustrates that when compared to the literature, theologians themselves do not always agree as to the viability of XTx, or as to the rationale appropriate to making the decision about the procedure. Nevertheless, the important takeaway is that a theologically informed XTx programme is one that has the greatest potential to maximize the benefit to their future patients, and more likely to have broad public support.

From an individual perspective, Judaism does not object to XTx to prolong and save human life, even with non-kosher animal donors with genetic modifications. The life we humans are graced with as a wondrous divine gift is a mortal one. The imperative of Deuteronomy, to “choose life” over curses and death, means that preserving life outweighs other values almost without exception. XTx, even from a pig, is welcome as a life-sustaining medical intervention from a Jewish ethical perspective.

In the Christian Tradition, the motivation is an attempt to follow the example of Jesus Christ in bringing healing to all those in need. While physiological healing is important, the ultimate goal is a person’s overall well-being which requires spiritual, mental and social well-being in addition to physical health. As human beings are already allowed, and even encouraged, to make use of animals to achieve greater human flourishing, XTx could be justified in terms of promoting human health as long as human dignity and integrity are preserved, animals are treated according to accepted ethical standards, and the overall risk/benefit ratio is presented to the patient.

The surest summative remark about Sunni Islamic bioethical perspectives on XTx would be that, given the state of the science, a definitive ethico-legal determination remains elusive. In general, one may advance that there would be contingent permisibility for XTx as a therapeutic modality given the following conditions: (i) non-porcine animals were the origin of organs, tissues and cells, (ii) these animals are treated with respect and well-cared for even if they are ultimately killed to be organ/tissue/cell donors, (iii) the therapeutic effects are life-saving and the health benefits of the treatment outweigh its harms, (iv) the recipient (or surrogate) is able to give informed consent based with sufficient understanding of the risks involved, and (v) the practice of XTx is available to society equitably. From the perspective of the three moral traditions, it must be acknowledged that XTx raises several theological issues that need to be considered before it is widely introduced. The ideas presented here suggest that each theological view provides the framework for evaluating the possible use of XTx—God’s call to bring healing to those in need, and a reasoning process to address the ethical issues it may present.

As suggested previously, the beliefs presented should not be considered as the final arbiter of collective theological thought for Jewish, Christian or Muslim followers. Rather, they illustrate the complex and at times competing nature that theological considerations entail compared to individual beliefs. Given the theological concerns associated with current survival probability, the potential costs that may constrain universal availability, and the use of porcine organs will require continuing deliberation within specific religious contexts. It is the authors’ hope that the information presented here provides a forum that stimulates further discussion and consideration of the importance of theological understanding and knowledge to the future development of clinical XTx.

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