BABOON HEARTS AND PIG LIVERS: ANTICIPATING THE FUTURE OF XENOTRANSPLANTATION AND ITS LEGAL RESPONSES

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ABSTRACT: The organ transplant shortage is a national public-health crisis leading to hundreds of thousands of deaths each year. Xenotransplantation, a procedure that involves the transplantation of animal organs, may be the most feasible solution to this issue. However, many unique risks are involved with xenotransplantation, namely the transmission of infectious diseases, known as xenozoonosis. Unknown risks, including the potential transmissions of infectious diseases unique to the procedure, pose potential violations of the Fourth and Fourteenth Amendments of the U.S. Constitution. To proceed with xenotransplantation trials, patients would need to give a "higher level" of informed consent for long-term surveillance, sample retrieval, quarantine, prohibitions on donating bodily tissues and fluids, and autopsies, among other restrictions. This Comment will discuss the issues and tensions of obtaining informed consent in xenotransplantation operations, consider how these issues can be addressed, and propose potential guidelines to obtain constitutional consent. This Comment will assert that despite constitutional challenges, informed consent can be obtained to enable the progression of xenotransplantation as a potential solution to the organ shortage crisis.

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On October 26, 1984, the heart of a seven-month-old baboon was transplanted for the first time into a human newborn.[1] She was widely known as Baby Fae, and she suffered from hypoplastic left heart syndrome, a congenital birth defect.[2] Without the baboon heart transplant, Baby Fae would have died immediately—but with the transplant, she survived for an additional twenty days.[3]

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1. Arthur L. Caplan, *Ethical Issues Raised by Research Involving Xenografts*, 254 JAMA 3339, 3339 (1985); *see also* Leonard Bailey, *Infant Heart Transplantation*, LOMA LINDA UNIV. HEALTH, https://lluh.org/leonard-bailey/infant-heart-transplantation [https://perma.cc/X9K6-VA8E].

2. Bailey, *supra* note 1.

3. *See generally* Leonard L. Bailey et al., *Baboon to Human Cardiac Xenotransplantation in a Neonate*, 254 JAMA 3321 (1985).

Despite Baby Fae's short life, the procedure demonstrated to scientists the potential of xenotransplantation[4] as a viable solution to the organ shortage crisis.[5] Over 104,000 people in the United States are currently waiting for a life-saving organ transplant.[6] On average, sixteen people die every day while waiting on the organ transplant list.[7] Another name is added to the organ transplant list every nine minutes.[8] Xenotransplantation may be the earliest and most feasible solution to reduce or eliminate loss of life due to organ scarcity. However, unique risks to xenotransplantation pose two challenges that this Comment seeks to address.

The first challenges that must be addressed before xenotransplantation can proceed are the Fourth and Fourteenth Amendment concerns that arise from asking a patient to commit to a life of medical surveillance. Although risks of infection exist within human-to-human organ transplants,[9] the full spectrum of infectious diseases that can be transmitted through xenotransplantation, namely xenozoonosis,[10] has yet to be researched in the same depth.[11] Because xenozoonosis can arise unexpectedly before, during, and after a transplantation, patients may need to be examined without prior notice and require regular medical surveillance, possibly for the rest of their lives. This extensive invasion of privacy will prompt an inevitable constitutional challenge that will require us to determine whether the government has a compelling interest in promoting xenotransplantation, and if so, whether the means to achieve that compelling interest are narrowly tailored to justify infringing upon a patient's fundamental rights.

Precedent indicates that xenotransplant patients can be analogized to individuals in other industries who voluntarily participate in a certain activity or occupation, thereby subjecting themselves to stricter regulations and reduced privacy expectations.[12] Further, in weighing a patient's privacy rights against

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4. The term *xenotransplantation* is defined by the Food and Drug Administration (FDA) as "any procedure that involves the transplantation, implantation or infusion into a human recipient of either (a) live cells, tissues, or organs from a nonhuman animal source, or (b) human body fluids, cells, tissues or organs that have had *ex vivo* contact with live nonhuman animal cells, tissues or organs." *See Xenotransplantation*, FOOD & DRUG ADMIN. (Mar. 3, 2021), https://www.fda.gov/vaccines-blood-biologics/xenotransplantation [https://perma.cc/FLJ2-MPX3]. However, this Comment will be referring to xenotransplantation generally as "the replacement, typically by a surgical operation, of a damaged or diseased vital organ or part . . . by a healthy version of the same organ from an animal . . . into a human being." *See* Jack M. Kress, *Xenotransplantation: Ethics and Economics*, 53 FOOD & DRUG L.J. 353, 353 (1998).

5. *See* Bailey, *supra* note 1.

6. *Facts and Myths About Organ Donation*, AM. TRANSPLANT FOUND., https://www.americantransplantfoundation.org/about-transplant/facts-and-myths/ [perma.cc/RXQ4-KYP8] (Jan. 12, 2023).

7. *Id.*

8. *Id.*

9. Draft Public Health Service (PHS) Guideline on Infectious Disease Issues in Xenotransplantation, 61 Fed. Reg. 49,920, 49,921–22 (Sept. 23, 1996).

10. Marian G. Michaels, *Xenozoonoses: The Risk of Infection After Xenotransplantation*, *in* LABORATORY ANIMAL MEDICINE (James G. Fox et al. eds., 2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7150069/pdf/main.pdf [https://perma.cc/LQ3U-HFBF].

11. *Cf.* 61 Fed. Reg. at 49,920–21.

12. *See generally* Vernonia Sch. Dist. 47J v. Acton, 515 U.S. 646 (1995); Skinner v. Ry. Labor Executives' Ass'n, 489 U.S. 602 (1989).

the government's compelling interest in protecting public health and promoting the progression of xenotransplantation, the government's interests will likely vastly outweigh any individual patient's interests. Ultimately, however, addressing the constitutional challenges of xenotransplantation alone is insufficient. Although the government likely has the power to compel xenotransplant patients to submit to lifelong medical surveillance and testing, the high level of commitment and invasion of bodily privacy of such testing demands additional patient consent that accommodates for these post-procedure requirements.

The second challenge to xenotransplantation is the insufficiency of the current regime of informed consent in addressing the needs of xenotransplantation. Generally, informed consent requires a clear and specific identification of the risks at play,[13] which is typically straightforward with average medical procedures. However, with xenotransplantation, the risks are not yet as clearly defined. The unknown risks associated with xenotransplantation render the traditional form of informed consent insufficient because xenotransplant patients will not know the likely consequences or relevant circumstances on which to base their consent.[14] Therefore, to encourage the progression of xenotransplantation, a new regime of informed consent should be adopted to ensure that patients understand they are consenting to lifelong medical scrutiny and a high level of privacy infringement.

This Comment will argue that xenotransplant patients *can* give this "higher level" of informed consent, which accommodates for the long-term medical surveillance that xenotransplantation demands. This includes testing and sample retrieval, possible quarantine, prohibitions on donating bodily tissues and fluids, and autopsy,[15] among other necessary medical procedures that may arise. Because the Food and Drug Administration (FDA) is currently devising plans to allow clinical trials for xenotransplantation to begin,[16] this Comment will advocate for judicial approval of xenotransplantation clinical trials with the implementation of a new regime of informed consent. The benefit of saving hundreds of thousands of people—who would otherwise die waiting for life-saving organs—vastly outweighs any intrusion on an individual xenotransplant recipient's privacy.

This Comment will proceed with Part I, which will examine the traditional model of informed consent and explain how this model is insufficient in meeting the needs of xenotransplantation. It will then consider the unknown risks of xenotransplantation and how a new model of informed consent can accommodate

13. *See generally Code of Medical Ethics Chapter 2: Opinions on Consent, Communication & Decision Making*, AM. MED. ASS'N, https://code-medical-ethics.ama-assn.org/chapters/consent-communication-decision-making [https://perma.cc/3AUN-54US] [hereinafter *AMA Code of Medical Ethics*].

14. Margaret A. Clark, *This Little Piggy Went to the Market: The Xenotransplantation and Xenozoonose Debate*, 27 J.L. MED. & ETHICS 137, 145 (1999).

15. *Id.*

16. Amy Dockser Marcus & Liz Essley Whyte, *FDA Planning to Allow Clinical Trials of Pig-Organ Transplants*, WALL ST. J., https://www.wsj.com/articles/fda-said-to-plan-pig-organ-transplant-clinical-trials-11656622411 [https://perma.cc/Q6TU-4GD6] (Jun. 30, 2022, 5:31 PM).

for these differences. Part II will discuss why this higher level of informed consent implicates both the Fourth and Fourteenth Amendments through case illustrations of *Skinner v. Railway Executives' Association*[17] and *Vernonia School District 47J v. Acton*.[18] Part III will propose solutions to these constitutional challenges and ultimately assert that this higher level of informed consent can be gained from xenotransplant patients. The Comment will then conclude by illustrating how these potential solutions will then allow xenotransplantation to move forward as the potential solution to the organ scarcity crisis.

I. THE CURRENT REGIME OF INFORMED CONSENT IS INSUFFICIENT FOR XENOTRANSPLANT PATIENTS

A. The Traditional Model of Informed Consent

The traditional process of informed consent has been designed for a variety of medical surgeries, operations, and procedures. Today, informed consent is defined by the Code of Medical Ethics Opinion 2.1.1 as when "communication between a patient and physician results in the patient's authorization or agreement to undergo a specific medical intervention."[19] Both patients and research subjects have a right to fully understand the logistics, risks, and benefits of a procedure, as well as any viable alternative options.[20] However, there has yet to be a situation in which a patient is required to give consent for lifelong medical surveillance, testing, and most importantly, impromptu emergency response to any unknown adverse symptoms or conditions that may appear after the procedure, potentially without notice. Naturally, the traditional process of gaining informed consent will have to be modified to include patient consent to the unknown possibilities of infectious pathogens and other long-term risks of xenotransplantation.

Traditional informed consent must also define the expected duration of the patient or subject's participation, which typically includes the procedure and recovery.[21] To properly obtain informed consent, the medical professional must assess the patient's ability to understand the information, consider the implications of the treatment and its alternatives, and document the informed consent on the patient's medical record.[22] Informed consent can also be withdrawn later if the patient decides not to go through with a procedure or the subject decides not to participate in a scientific research trial.[23] Finally, informed consent does not ordinarily need to be obtained from the patient's intimate partners, family, or other close contacts. In fact, "[a] patient's independence" to make an autonomous decision regarding the patient's body is traditionally "the highest priority

17. 489 U.S. 602 (1989).
18. 515 U.S. 646 (1995).
19. *AMA Code of Medical Ethics*, *supra* note 13.
20. *Id.*
21. 21 C.F.R. § 50.25(a)(1) (2022).
22. *AMA Code of Medical Ethics*, *supra* note 13.
23. 45 C.F.R. § 46.116(b)(8) (2022).

in American bioethics."[24] As a result, obtaining informed consent from third parties on behalf of the patient or subject of a procedure can be seen as violating the patient's autonomy, as it infringes on an individual's autonomous decision-making abilities.[25]

B. The Risks of Xenotransplantation

The limited research surrounding the risks of infectious disease transmission through xenotransplantation renders the traditional process of informed consent insufficient. There are many historical instances in which scientists and experts in viral research have not accurately predicted how these diseases would behave and manifest within humans. One example of cross-species disease transmission was seen during the AIDS epidemic, in which scientists found the HIV-1 virus to be non-virulent in chimpanzees, but highly contagious in humans.[26] Because scientists did not have adequate technology to detect and study the virus, the situation was even more alarming when AIDS began appearing among humans.[27] Another example of an infectious disease is called porcine endogenous retrovirus, or PERV, which is found in pig cells.[28] Scientists have observed PERV infecting human cells in vitro.[29] Despite a lack of issues in survivors of porcine pancreatic islet cell transplantations to date, there is no data proving these infectious diseases will not have a more sudden, disparate impact on human patients in a more invasive and dangerous procedure such as xenotransplantation.[30]

Further, xenozoonosis can also stem from poor donor animal safety protocols.[31] Despite tentative FDA Guidance for Industry regarding animal donors' screening, evaluation, and testing, no formal regulations have been officially implemented.[32] During a Cellular, Tissue, and Gene Therapy Advisory Committee Meeting in June 2022, the FDA discussed potential regulations to create multiple levels of safety for donor animals, citing potential regulations such as breeding animals from closed herds of known origin; maintaining their health

24. Laura Sedig, *What's the Role of Autonomy in Patient- and Family-Centered Care When Patients and Family Members Don't Agree?*, 18 AM. MED. J. ETHICS 11, 13 (2016), https://journalofethics.ama-assn.org/sites/journalofethics.ama-assn.org/files/2018-05/ecas2-1601.pdf [https://perma.cc/T425-BZ3K].

25. *See id.* at 13–14.

26. *E.g.*, Jocelyn A. Holland, *The "Catch-22" of Xenotransplantation: Compelling Compliance with Long-Term Surveillance*, 7 HOUS. J. HEALTH L. & POL'Y 151, 154–55 (2006).

27. *Id.* at 154.

28. Clark, *supra* note 14, at 139 (citing R. Weiss, *Study Finds Danger from Pig Transplants*, HOUS. CHRON., Oct. 17, 1997, at 14; P. Le Tissier et al., *Two Sets of Human-Tropic Pig Retrovirus*, 389 NATURE 681, 681–82 (1997)).

29. *Id.*

30. *See id.*

31. *See* U.S. FOOD & DRUG ADMIN., SOURCE ANIMAL, PRODUCT, PRECLINICAL AND CLINICAL ISSUES CONCERNING THE USE OF XENOTRANSPLANTATION PRODUCTS IN HUMANS: GUIDANCE FOR INDUSTRY, https://www.fda.gov/media/102126/download [https://perma.cc/8MRP-9P4J] (Dec. 2016).

32. *See id.*

in appropriate facilities; quarantining donor animals before harvest; documenting the harvest and handling of donor animal cells, tissues, and organs; and archiving samples of the donor animal before and after harvest.[33]

Nonetheless, the FDA remains cautious about fully pursuing xenotransplantation clinical trials in part because of the lack of official implementation of these regulations.[34] During this Committee Meeting, the FDA raised other concerns associated with xenotransplantation, such as adverse inflammatory and immunological responses to donor cells or secreted molecules; detrimental effects due to potential rejection of donor animal cells, tissues, or organs; physiological and metabolic incompatibility; and deleterious effects from the use of immunosuppressive agents.[35] In particular, one of the most recently authorized xenotransplantation trials illustrates the increased risk of immunosuppressive agents facilitating pathogen transmission.[36]

C. David Bennett—Tragic Lessons Learned

In January 2022, at the University of Maryland Medical Center, surgeons successfully transplanted a genetically modified pig heart into a living patient for the first time in history.[37] The heart had ten genetic changes to make it more compatible with the human body[38] and was tested for pathogens, including a pig virus called porcine cytomegalovirus (pCMV).[39] The patient, David Bennett, was in end-stage heart failure, which disqualified him from receiving a human

33. Judith Arcidiacono, *FDA Views on Xenotransplantation: Cellular, Tissue, and Gene Therapy Advisory Committee Meeting (CTGTAC)*, FOOD & DRUG ADMIN. 11 (June 29, 2022), https://www.fda.gov/media/159535/download [https://perma.cc/YF7B-AWV5].

34. *Cf*. *id*. 3-4.

35. *Id.* at 7.

36. Shiyang Zhang, *Cardiac Xenotransplantation: A First In-Human Experience*, AM. COLL. CARDIOLOGY (Mar. 1, 2022), https://www.acc.org/Membership/Sections-and-Councils/Fellows-in-Training-Section/Section-Updates/2022/03/01/20/45/Cardiac-Xenotransplantation [https://perma.cc/4C5C-JA7V].

37. Jason Mast, *In Historic First, Surgeons Transplant a Genetically Modified Pig Heart into a Dying Patient*, ENDPOINTS NEWS, https://endpts.com/in-historic-first-surgeons-transplant-a-genetically-modified-pig-heart-into-a-dying-patient/ [https://perma.cc/TJG2-Q2F4] (Jan. 11, 2022, 10:12 AM).

38. Scientists eliminated three genes from the pig's genome that could lead to organ rejection, introduced six human genes to help the patient's body accept the new heart, and eliminated one more gene that would prevent the pig's heart from growing too large. *See* Kevin Doxzen, *In a Medical First, a Gene-Edited Pig Heart Has Been Transplanted into a Human Patient*, WORLD ECON. F. (Jan. 19, 2022), https://www.weforum.org/agenda/2022/01/gene-edited-pig-heart-transplanted-into-human-patient/ [https://perma.cc/ER9M-9EVH].

39. Elisha Fieldstadt, *First Man to Receive a Transplanted Pig Heart Died of Heart Failure, Not Rejection, Encouraging Doctors*, NBC NEWS (July 7, 2022, 7:52 AM), https://www.nbcnews.com/health/heart-health/first-man-receive-transplanted-pig-heart-died-heart-failure-not-reject-rcna37078 [https://perma.cc/P995-4ZG5]. pCMV, or porcine cytomegalovirus, is a viral infection that is present in nearly all swine. pCMV can be latent and become reactivated at later points in a pig's life. Currently, there is no vaccine for pCMV, and a high mortality rate is observed in neonates that develop this disease. *See Porcine Cytomegalovirus* CTR. FOR FOOD SEC. & PUB. HEALTH (Dec. 2015), https://www.swinehealth.org/wp-content/uploads/2021/08/shic-factsheet-porcine-cytomegalovirus.pdf [https://perma.cc/5PNP-LKSG].

heart through the traditional organ donor system.[40] The FDA approved the xenotransplantation procedure under compassionate use, an emergency measure used to allow patients with no other medical options to participate in experimental procedures.[41] The procedure was initially successful, as the patient's body did not reject the transplanted organ.[42] However, Bennett tragically passed just two months later.[43] During the autopsy, it was discovered that the cause of death was not organ rejection as originally believed, but rather heart failure.[44] Despite rigorous infection control measures before, during, and after transplantation, the heart was infected with pCMV, one of the pathogens the heart was tested for before transplantation.[45]

Scientists are debating possible explanations for the ultimate heart failure, but one of the main theories is that the presence of pCMV likely caused inflammation, which "contributed to the cascade of events that caused his death."[46] The pCMV may have also established itself in the body because of the immunosuppressive drug the patient was required to take to prevent rejection of the heart,[47] which increases the risk of disease transmission.[48] Because xenotransplantation bypasses many of the patient's protective immunological and physical barriers, and because it requires the ingestion of an immune-system-suppressing drug, a patient's long-term survival can be put at risk by infectious agents.[49] The FDA's concern about the heightened risk from the interaction of immunosuppressive agents and xenozoonosis manifested in Bennett's situation—showing that the FDA's fears were not unfounded.[50]

Bennett's procedure illustrates that a xenotransplant recipient will likely have to cooperate with follow-up studies for many years, if not the rest of their lives.[51] Any unexplained symptom or condition could potentially lead to the discovery of a new infectious disease.[52] Bennett's case illustrated not only how quickly unknown medical emergencies can arise after the procedure, but also how quickly a patient's health can deteriorate if professionals cannot respond to and treat the condition in a timely manner. Giving medical professionals the

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40. Mast, *supra* note 37. Patients with serious heart disease can be denied for organ transplant candidacy due to the high level of fatality associated with the illness and the invasiveness of the transplant operation. *See The Kidney Transplant Waitlist—What You Need to Know*, NAT'L KIDNEY FOUND., https://www.kidney.org/atoz/content/transplant-waitlist#what-would-prevent-or-disqualify-me-receiving-transplant-does-my-age-matter [https://perma.cc/8EXN-VPFY].

41. Zhang, *supra* note 36.

42. Amy Dockser Marcus, *Death of Man Who Received a Pig-Heart Transplant Remains a Mystery*, WALL ST. J., https://www.wsj.com/articles/death-of-man-who-received-a-pig-heart-transplant-remains-a-mystery-11655933404 [https://perma.cc/PBR2-UUHM] (June 22, 2022, 6:19 PM).

43. Fieldstadt, *supra* note 39.

44. *Id.*

45. *Id.*

46. Marcus, *supra* note 42.

47. *Id.*

48. Fieldstadt, *supra* note 39.

49. Marcus, *supra* note 42; *see also* Roumiana S. Boneva et al., *Infectious Disease Issues in Xenotransplantation*, 14 CLINICAL MICROBIOLOGY REVS. 1, 11 (2001).

50. Arcidiacono, *supra* note 33.

51. Clark, *supra* note 14, at 145.

52. *Id.*

opportunity to catch these conditions in the early stages is imperative to a patient's health, as once there is a need for exigency, it may be too late. As a result, this high level of medical scrutiny leads us back to the crucial question of addressing this high level of infringement on a patient's bodily autonomy and right to privacy. This requires a new regime of informed consent that notifies patients about the unknown risks of xenozoonosis and the possibility of unexpected conditions arising at any time.

D. Informed Consent on Behalf of Third Parties

This higher level of informed consent to undergo lifelong medical surveillance should also ideally strive to include the patient's close contacts. After a xenotransplantation procedure, the patient will likely be around close friends, family, and healthcare workers, increasing the risk of xenozoonosis.[53] The Public Health Service released a draft of a Guideline on Infectious Disease Issues in Xenotransplantation in August 1996, which discusses specific measures the patient should undertake to prevent transmission of xenozoonosis to others, such as refraining from sexual intercourse or donating blood and other tissue.[54] The risk of infectious pathogens spreading to others may be the strongest reason to advocate for informed consent to include third parties in medical surveillance such as the patient's intimate partners, family members, and healthcare workers involved in the xenotransplantation procedure and subsequent monitoring.

However, there is a lack of precedent that supports the idea of gaining informed consent to undergo lifelong medical surveillance from a patient on behalf of their close contacts. Currently, the only acceptable circumstances to obtain informed consent on behalf of another are if the patient is a minor,[55] is incapacitated due to a medical condition or disorder, or has previously designated a surrogate to make decisions on the patient's behalf.[56] These narrow exceptions are unlikely to justify allowing a xenotransplant patient to consent on behalf of all the patient's current and future contacts. Further, individuals' constitutional right to bodily self-autonomy is held paramount in American society. The idea of one person consenting on another's behalf contradicts the fundamental right that each individual in this country inherently possesses autonomy over the individual's being.

The discussion about gaining informed consent from third parties who could be in contact with the xenotransplant patient is obviously a vast and contested domain and would require much more scholarship to engage this field responsibly. This, however, is beyond the scope of this Comment. Rather, due to the lack of precedent that allows giving informed consent on behalf of others,

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53. Draft Public Health Service (PHS) Guideline on Infectious Disease Issues in Xenotransplantation, 61 Fed. Reg. 49,920 (Sept. 23, 1996).

54. *Id.*

55. *See* Ann McNary, *Consent to Treatment of Minors*, 11 INNOVATIONS CLINICAL NEUROSCI. 43, 43–44 (2014), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4008301/pdf/icns_11_3_43.pdf [https://perma.cc/4H94-NKGG].

56. *See* CODE OF MED. ETHICS OP. 2.1.2: DECISIONS FOR ADULT PATIENTS WHO LACK CAPACITY (AM. MED. ASS'N 2016).

the issue will have to be closely monitored as xenotransplantation progresses for a more specific solution.

II. PRECEDENT ON INFORMED CONSENT IN XENOTRANSPLANTATION

Because the government will mandate lifelong medical surveillance of xenotransplant patients due to the inherent risks of the procedure, there are inevitable constitutional challenges that must, in turn, be overcome. Specifically, this high level of invasion of xenotransplant patients' privacy raises Fourth and Fourteenth Amendment challenges.

First, the Fourth Amendment provides "the right of the people to be secure in their *persons*, houses, papers, and effects, *against unreasonable searches and seizures*."[57] The Supreme Court has long ruled that this definition of a search extends to when state actors seek to obtain physical evidence from an individual, such as through blood tests to analyze alcohol content.[58] Therefore, the lifelong medical scrutiny that a xenotransplant patient will have to consent to can be considered a lifelong search under the pretense of the Fourth Amendment.

Next, the Fourteenth Amendment provides that "no state shall make or enforce any law which shall abridge the privileges or immunities of citizens of the United States; nor shall any State *deprive any person of life, liberty, or property, without due process of law*."[59] Because lifelong medical scrutiny infringes on a patient's fundamental autonomy and privacy interests, the governing standard to pass constitutional muster is strict scrutiny.[60] Therefore, the compelling government interest must be advanced through narrowly tailored means to justify the infringement upon the individual's rights.[61]

Unfortunately, it is likely that the lack of knowledge about the spectrum of risks renders xenotransplant patients unable to constitutionally waive their rights under the Fourth or Fourteenth Amendments. For example, in *Brady v. United States*, the Supreme Court held that "[w]aivers of constitutional rights not only must be voluntary but must be knowing, intelligent acts done with *sufficient awareness of the relevant circumstances* and *likely consequences*."[62] Xenotransplant patients' inability to validly waive their rights can be analogized with suspects who invalidly waive their *Miranda* rights.[63] For suspects to

57. U.S. CONST. amend. IV (emphasis added).

58. Schmerber v. California, 384 U.S. 757, 767–68 (1966).

59. U.S. CONST. amend. XIV, § 1 (emphasis added).

60. Planned Parenthood of Southeastern v. Casey, 505 U.S. 833, 871 (1992), *overruled* by Dobbs v. Jackson Women's Health Org., 142 S. Ct. 2228 (2022).

61. *Id.*

62. Brady v. United States, 397 U.S. 742, 748 (1970) (emphasis added).

63. *Miranda* rights were created to protect a suspect's Fifth Amendment's right against self-incrimination and bars the admission of coerced, incriminating statements. *See generally* Miranda v. Arizona, 384 U.S. 436 (1966).

properly waive their *Miranda* rights, they must not only "know their rights in the abstract, they must have *understood* them."[64]

Because a medical professional cannot surely tell a xenotransplant patient what the patient's relevant circumstances and likely consequences will be after the procedure, the patient's lack of understanding leads to the conclusion that the patient cannot give an intelligent, knowing, and constitutional waiver of rights. Therefore, we must examine whether these challenges survive constitutional muster through the tests set forth in the caselaw. Ultimately, the two cases discussed and summarized below illustrate that these constitutional challenges *can* be addressed and that this higher level of informed consent *can* be properly obtained from xenotransplant patients.

A. *Skinner v. Railway Executives' Association* (1989)

In *Skinner v. Railway Executives' Association*, the Supreme Court held that government regulations mandating biological samples from public industry employees without reasonable suspicion do not violate the Fourth Amendment[65] because compelling government interests and needs render probable cause and warrant requirements unfeasible.[66] In this case, the Federal Railroad Administration (FRA) authorized breath, blood, and urine tests.[67] Employees who were involved in train accidents, violated certain rules, or raised some other reasonable, individualized suspicion that they were under the influence of alcohol or drugs while operating trains were required to take these tests.[68] The Railway Labor Executives' Association brought suit against the FRA, claiming that these drug and alcohol test mandates violated the employees' Fourth Amendment rights.[69]

Justice Kennedy delivered the majority opinion by first discussing the text of the Fourth Amendment.[70] From there, he turned to the question of whether the activity was conducted by a state actor, which triggers a Fourth Amendment analysis.[71] The Court held that "the fact that the government has not compelled a private party to perform a search does not, by itself, establish that the search was a private one."[72] The government only needs to encourage and endorse the activity to trigger the Fourth Amendment.[73] Then, Justice Kennedy emphasizes that "compelled intrusio[ns] into the body" for urine and blood tests must be deemed a Fourth Amendment seizure,[74] as this "physical intrusion, penetrating

64. Alameda Cnty. Dist. Att'y's Off., *Miranda Waivers*, POINT VIEW, Winter 2013, at 1, 4, https://www.unco.edu/project-climb/pdf/toolkit/resources-publications/da-office-miranda-waivers.pdf [https://perma.cc/U6ZF-NGVS].

65. Skinner v. Ry. Labor Executives' Ass'n, 489 U.S. 602, 633 (1989).

66. *Id.* at 623.

67. *Id.* at 606.

68. *Id.* at 611.

69. *Id.* at 612.

70. *Id.* at 613–14.

71. *Id.* at 614.

72. *Id.* at 615.

73. *Id.* at 615–16.

74. *Id.* at 616 (quoting Schmerber v. California, 384 U.S. 757, 767–68 (1966)).

beneath the skin, infringes an expectation of privacy that society is prepared to recognize as reasonable."[75]

However, Justice Kennedy is quick to point out that not all seizures are barred under the Fourth Amendment, but only the unreasonable ones.[76] A seizure is determined to be reasonable based on the circumstances and nature of the seizure—therefore, the test to determine whether a seizure is constitutional is "judged by balancing its intrusion on the individual's Fourth Amendment interests against its promotion of legitimate government interests."[77] Typically, this balance is struck in favor of the procedures described by the Warrant Clause of the Fourth Amendment; however, as in the instant case, there are exceptions to this rule where "special needs . . . make the warrant and probable-cause requirement impracticable."[78] Often, the Warrant Clause may actually hinder the governmental purpose behind the seizure and does little to further protect privacy interests.[79] Ultimately, the Court held that the government's compelling interest in public safety would be unduly burdened if the FRA had to abide by the Warrant Clause before testing an employee.[80]

Moreover, the Court emphasized that the tests were not an undue intrusion on an individual's privacy and bodily integrity.[81] It was determined that these tests were performed in a reasonable manner, as they were conducted by a physician within a hospital environment according to proper medical procedure.[82] The tests also only identified certain controlled substances within the employees and did not disclose any "other facts in which the employee has a substantial privacy interest."[83] Finally, the Court also emphasized that railroad employees had a lower expectation of privacy due to their voluntary "participation in an industry that is regulated pervasively to ensure safety, a goal dependent, in substantial part, on the health and fitness of covered employees."[84]

B. *Vernonia School District 47J v. Acton* (1995)

In *Vernonia*, the Supreme Court held that student athletes may be tested for drugs without reasonable suspicion or a warrant because students participating in the athletic program voluntarily subject themselves to a higher level of scrutiny and therefore, a lesser expectation of privacy.[85] In this case, a school's Student Athlete Drug Policy required students who participated in school athletic programs to sign a consent form for random urinalysis drug testing.[86] This policy came into play in response to the sharp increase in student drug use, which

75. *Id.*
76. *Id.* at 619.
77. *Id.* (quoting Delaware v. Prouse, 440 U.S. 648, 654 (1979)).
78. *Id.* (quoting New Jersey v. T.L.O., 469 U.S. 325, 351 (1985)).
79. *See id.* at 622–23.
80. *Id.* at 633.
81. *Id.* at 625.
82. *Id.*
83. *Id.* at 626.
84. *Id.* at 627.
85. Vernonia Sch. Dist. 47J v. Acton, 515 U.S. 646, 666 (1995).
86. *Id.* at 650.

in turn led to an increase in student discipline and sports-related injuries.[87] Respondent Acton refused to sign a consent form to be tested and was therefore barred from participating in the sports program.[88] He filed suit, alleging that the policy violated the Fourth and Fourteenth Amendments.[89]

Justice Scalia's majority opinion held that the Student Athlete Drug Policy was constitutional.[90] In coming to this conclusion, Justice Scalia used the *Skinner* test, which determines whether a search meets the reasonable standard by weighing the intrusions on the individual's Fourth Amendment rights against the promotion of compelling government interests.[91] Justice Scalia began by considering the nature of the individual's privacy interest at stake, stating that "[p]articularly with regard to medical examinations and procedures . . . 'students within the school environment have a lesser expectation of privacy than members of the population.'"[92] Moreover, student athletes have even lesser privacy expectations than students generally—by choosing to "go out for the team," they must comply with a physical examination, have adequate insurance or sign an insurance waiver, maintain a minimum grade point average, and follow "rules of conduct, dress, training hours and related matters as may be established for each sport."[93] He analogized student athletes to adults who voluntarily choose to work in a highly regulated industry, such as the railroad industry in *Skinner*, and therefore should reasonably expect intrusions on their privacy because of the nature of the activity.[94]

Justice Scalia then discussed various factors that affect the degree of privacy intrusion by the urinalysis tests, and that the degree of intrusion depends heavily on the manner in which the tests are conducted.[95] The results of the urinalysis tests weigh toward a finding of negligible privacy interest, as they only disclose findings of certain controlled substances and do not reveal information on other medical conditions, such as whether the student is pregnant or diabetic.[96] Finally, the test results are only made available to limited school authorities who need to know whether the student is violating the policy, and the results are not given to law enforcement for further discipline.[97] Cumulatively, these pertinent factors create a negligible intrusion of privacy, which aligns with the lesser expectation of privacy student athletes have.

The next step of the *Skinner* test weighs the school's compelling interest in deterring drug use against the students' individual privacy values to determine

87. *Id.* at 649.
88. *Id.* at 651.
89. *Id.* at 648.
90. *Id.* at 664–65.
91. *Id.* at 652–53.
92. *Id.* at 656–57 (quoting New Jersey v. T.L.O., 469 U.S. 325, 348 (1985)).
93. *Id.* at 657.
94. *Id.*
95. Boys produce samples at a urinal, and although they are watched by a monitor of the same sex, they are fully clothed. Girls are monitored by a female outside an enclosed bathroom stall. Justice Scalia asserts that these conditions are "nearly identical" to conditions typically experienced by people in public restrooms, and therefore, the privacy intrusion is negligible. *Id.* at 658.
96. *Id.*
97. *Id.*

whether the school's interest is sufficiently weighty to warrant such intrusions. Generally, the school has a compelling interest in student health and safety.[98] More importantly, the school has a specific interest in addressing the sharp increase in drug use in the student body through randomized drug tests because, comparable to adults, drug use exacerbates the health of school children.[99] Justice Scalia held that these compelling interests were adequately served by the narrowly tailored means of the drug tests and vastly outweighed any minimal intrusion on students' privacy, therefore rendering the Student Athlete Drug Policy constitutional.

C. Implementing a Warrant or Individualized Suspicion Requirement for Xenotransplant Patients Is Unduly Burdensome

The unexpected demands of xenotransplantation are not compatible with an individualized or reasonable suspicion requirement. The requirement for lifelong medical surveillance is essential in serving the government's compelling interests of preventing a potential public health crisis. As the Supreme Court found in *Skinner*, "The government's interest in dispensing with the warrant requirement is at its strongest when . . . 'the burden of obtaining a warrant is likely to frustrate the governmental purpose behind the search.'"[100] If a patient develops a post-procedural, adverse side effect, remedial measures should be undertaken expeditiously before the condition worsens. Delaying examinations on the basis of a warrant wastes precious time that medical professionals can use to diagnose and treat the patient's symptoms or conditions. Further, the time spent waiting for a warrant could allow the disease to spread. As illustrated in Bennett's situation, a xenotransplant procedure's initial success is not the endgame. Post-procedural examinations are at least as critical to a patient's long-term welfare as the operation itself.

This situation contrasts with *Skinner*, where railroad employees were compelled to undergo drug tests only after they were involved in a train accident, or the employer had individualized suspicion to believe the employee was under the influence of drugs or alcohol while on the job. With xenotransplant patients, requiring some sort of reasonable suspicion that a patient is experiencing an adverse side effect after the procedure can cause the disease to progress, rather than being treated initially. Further, if a new regime of informed consent is implemented, the patient will be informed as part of their consent to the procedure that emergency measures will need to be taken if necessary. Preemptive surveillance will allow medical professionals to address medical emergencies as soon

98. *See id.* at 656–57.

99. *Id.* at 660–63. At the students' young age, "maturing nervous systems are more critically impaired by intoxicants than mature ones are . . . [and] children grow chemically dependent more quickly than adults, and their record of recovery is depressingly poor." *Id.* at 661 (citing Hawley, *The Bumpy Road to Drug-Free Schools*, 72 PHI DELTA KAPPAN 310, 314 (1990)).

100. Skinner v. Ry. Lab. Executives' Ass'n, 489 U.S. 602, 623 (1989) (quoting Camara v. Mun. Ct. of S.F., 387 U.S. 523, 533 (1967)).

as possible, rather than waiting for symptoms to manifest to fulfill the requirement of reasonable suspicion. Therefore, implementing either a warrant or individualized suspicion requirement is unfeasible, unsafe, and unduly burdensome for xenotransplantation procedures.

III. PROPOSED SOLUTIONS TO OVERCOME THE CONSTITUTIONAL CHALLENGES IN XENOTRANSPLANTATION

A. A Fourth Amendment Response

Xenotransplant recipients will likely be mandated to commit to lifelong surveillance, testing, and evaluation after the procedure due to xenozoonosis risk. This requirement for lifelong medical surveillance will likely implicate similar Fourth Amendment concerns as those in *Skinner* and *Vernonia*. The *Skinner* test determines whether a medical surveillance mandate survives constitutional muster is determined by the *Skinner* test. This test weighs the government's compelling interests in minimizing the risk of xenozoonosis and promoting xenotransplantation as a solution to the organ shortage crisis, against the patient's individual privacy and bodily autonomy rights.

The first step in Fourth Amendment analysis requires us to determine if there is a state actor. As FDA approval of clinical trials of xenotransplantation looming on the horizon, federal funding is very likely to follow.[101] Consequently, researchers who participate in these clinical trials would be considered government actors.[102] Even without federal funding, *Skinner* held that the government need not compel a private party to perform. Instead, even encouraging or endorsing an activity is sufficient.[103] Therefore, FDA approval alone likely satisfies the government actor requirement.

The next step in the *Skinner* test is to examine the aspects of both the government's and the patient's compelling interests and determine if one outweighs the other. Regarding the patient's compelling interests, the voluntary nature of xenotransplantation arguably helps address the challenges to obtaining informed consent arising under the Fourth Amendment. As in *Skinner*, where railroad employees chose to voluntarily work in an industry where safety is contingent on employee fitness and welfare, patients undergoing a xenotransplant procedure voluntarily consent to a high level of medical scrutiny by agreeing to the procedure. Xenotransplant patients likely consent to the procedure in the first place because they are unable to find a matching donor or are disqualified from the organ donor list through the traditional organ donation and transplantation process.

On the other hand, there is a distinction in the voluntary nature between an employee choosing to work in a particular industry and a patient deciding whether to undergo life-saving treatment. However, simply because the stakes are higher in a xenotransplant patient's situation than a railroad worker's does

101. *See* Holland, *supra* note 26, at 160.
102. *Id.*
103. *Skinner*, 489 U.S. at 615.

not necessarily make the patient's choice less voluntary. Like other high-risk medical procedures, xenotransplantation patients must carefully consider their ability to commit to a life of medical surveillance and restrictions before coming to a decision. Any invasive procedure that prolongs life, not just xenotransplantation, has this same tension where patients must weigh the possibility that their quality of life may be diminished after pursuing treatment. Patients with terminal cancer who decide to undergo chemotherapy are never seen as coerced into the treatment. Those same patients can also deny treatment and choose to live out the rest of their days with what they have. Both decisions are equally voluntary, and xenotransplantation is no different.

Next, the minimal degree of intrusion of the post-procedure examinations can further explain how the government's compelling interests outweigh a patient's compelling interests. In both *Vernonia* and *Skinner*, the Court emphasized that the drug tests' degree of intrusion was negligible because they were conducted in accordance with proper medical procedures by physicians or other authorized medical personnel in a hospital environment.[104] Further, the information gathered was specifically limited to controlled substances and did not disclose any other conditions that could be considered a higher invasion of privacy.[105] For xenotransplant patients, post-procedure examinations would be conducted similarly. Medical personnel would likely take blood samples rather than a more intrusive sample, such as excretion, and do so in a hospital setting rather than a more public one.[106] This method would also lessen the embarrassment and humiliation factors that typically raise the degree of intrusion in a Fourth Amendment analysis. Further, the results of these examinations would be limited to potential infections and diseases, rather than nonrelevant health conditions.[107] The results would not be available to the public, but instead they would only be accessible to a limited number of authorized personnel, such as scientists and doctors who are intimately familiar with the patient and the procedure.

Opposers may argue that post-procedural surveillance for xenotransplant patients may be more intrusive than the testing at issue in *Vernonia* and *Skinner* because of its lifelong duration and potential for greater restrictions, such as quarantine. However, accepting larger risks for a life-saving procedure like xenotransplantation is arguably reasonable, especially in a post-COVID world where quarantine, tissue sampling, and other examinations are often used as preventative measures to combat disease transmission. Although it is true that lifelong medical testing is a larger commitment than the tests seen in *Skinner* and *Vernonia*, it likely has little bearing on the cost-benefit analysis between the government's and patients' compelling interests, as the government's value in protecting public health vastly outweighs a patient's commitment to medical surveillance. Ultimately, the patient's rights to privacy and bodily autonomy are

104. *Cf. Vernonia*, 515 U.S. at 658; *Skinner*, 489 U.S. at 625.

105. *Vernonia*, 515 U.S. at 658; *Skinner*, 489 U.S. at 626.

106. Draft Public Health Service (PHS) Guideline on Infectious Disease Issues in Xenotransplantation, 61 Fed. Reg. 49,920, 49,926 (Sept. 23, 1996).

107. *Id.* at 49,920.

greatly outweighed by the government's compelling interests once examined through the *Skinner* lens. This aids in the constitutional analysis in justifying proceeding with xenotransplantation trials.

B. Bodily Autonomy Substantive Due Process Objections

Challenges to gaining informed consent for xenotransplantation arising under the Substantive Due Process Clause of the Fourteenth Amendment can be addressed as well. Under the Fourteenth Amendment, government actions that burden a fundamental right to life, liberty, or property interest, even if they are not explicitly listed within the Constitution, are subject to strict scrutiny.[108] Therefore, unless the means are narrowly tailored to achieve a compelling government interest, such actions do not pass constitutional muster.[109] Although it is debatable whether xenotransplant patients' privacy implications fall under strict scrutiny, lifelong medical surveillance is a heavy burden that must be weighed against a legitimate compelling interest.

The best caselaw advocating for medical privacy as a fundamental right can be found in *Griswold v. Connecticut*. In this case, the Supreme Court ruled that the rights to personal autonomy, bodily integrity, self-dignity, and self-determination all justify a fundamental right to contraception under the Due Process Clause in the Constitution.[110] The Court emphasized that the right to privacy, and therefore the right to contraception, can be inferred from the penumbras, or the "shadowy edges," of rights that are enumerated.[111] Similarly, it can be argued that xenotransplant patients' right to be free of lifelong medical scrutiny is likely to fall within the penumbras of the enumerated rights. As a result, compelling xenotransplant recipients to commit to lifelong medical surveillance may violate the individuals' fundamental right to privacy as guaranteed under substantive due process.[112]

Therefore, the next question to be asked in analyzing substantive due process in this scheme is whether the infringement on patients' privacy passes constitutional muster. To pass strict scrutiny, the means must be narrowly tailored to achieve a compelling government interest.[113] Here, it is clear that the Government's compelling interest in preserving public health and preventing xenozoonosis transmission outweighs the negligible privacy intrusions that patients will experience. Because of the unknown nature of infectious diseases from animal organs and the range of possible symptoms and long-term effects of the procedure, failing to conduct these evaluations after the procedure could be dangerous not only to the patient, but to greater society as well. Moreover, the government has a compelling interest in exploring and encouraging xenotransplantation as the solution to saving lives lost due to the organ shortage crisis.

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108. *See* Planned Parenthood of Southeastern Pa. v. Casey, 505 U.S. 833, 871 (1992), *overruled by* Dobbs v. Jackson Women's Health Org., 142 S. Ct. 2228 (2022).

109. *Id.*

110. *See* Griswold v. Connecticut, 381 U.S. 479, 485–86 (1965).

111. *Id.* at 484.

112. Holland, *supra* note 26, at 160.

113. *See Casey*, 505 U.S. at 871.

Although lifelong medical surveillance seems to be counterintuitive to the concept of a narrowly tailored means, this method is likely the only way the government can protect the health of both the patient and the public, especially while the extent of infectious diseases risks is still largely unknown. As xenotransplantation progresses, the length and types of medical examinations conducted can be adjusted and reduced accordingly, as we discover which tests are necessary and which are not. Further, despite the lifelong commitment to testing, the low level of intrusiveness of the proposed examinations illustrates the government's effort to minimize the privacy infringement aspect as much as possible. Finally, the Supreme Court has been deferential to the government's decisions on public health legislation for decades and should be no different with xenotransplantation.[114] Ultimately, courts can find that while the monitoring, testing, and evaluation of xenotransplant recipients may infringe on their privacy and bodily integrity, the government's compelling interests behind these evaluations justify constitutional approval.

Although the contours of the debate on the substantive due process rights of xenotransplant patients have yet to be fully fleshed out, xenotransplantation trials must progress to respond to the massive loss of life from the organ shortage. Despite a lack of precedent dictating whether post-procedure monitoring requirements for xenotransplantation patients are subject to strict scrutiny, it is clear that either way, carefully enacted legislation outlining how to obtain informed consent from xenotransplantation patients can survive the Fourth and Fourteenth Amendment challenges. FDA approval of xenotransplantation is inevitable[115] and courts must begin to formulate a response to the informed consent issue as soon as possible.

Advances in understanding the science behind xenotransplantation as well as potential solutions to the risks associated with the procedure have moved the FDA to devise plans to authorize clinical trials.[116] In August 2023, New York University's (NYU's) Langone Health announced that surgeons transplanted a pig kidney into a brain-dead patient, and the kidney has functioned appropriately "for over a month."[117] The director of NYU Langone's transplant institute, Dr. Robert Montgomery, has stated that the "[the pig kidney] looks even better than a human kidney."[118] The University of Alabama reported a similarly successful experiment in August 2023 in which "a pair of pig kidneys worked normally inside another donated body for seven days."[119] Because of these experiments,

114. *See* Patrik S. Florencio & Erik D. Ramanathan, *Are Xenotransplant Safeguards Legally Viable?*, 16 BERKELEY TECH. L.J. 937, 968 (2001).

115. *See* Marcus & Whyte, *supra* note 16.

116. *Id.*

117. Associated Press, *Pig Kidney Works in a Brain-Dead Man for over a Month, a Step Toward Animal-Human Transplants*, NBC NEWS (Aug. 16, 2023, 5:07 PM), https://www.nbcnews.com/health/health-news/pig-kidney-transplant-human-rcna100098 [https://perma.cc/NP5A-2VHV].

118. *Id.*

119. *Id.*

the FDA will be "considering whether to allow . . . pig heart or kidney transplants in volunteer patients."[120] Therefore, as xenotransplantation clinical trials are inevitably set to proceed, the time is ripe to discuss how to obtain proper informed consent from the patient that protects the patient as well as greater society before the procedure becomes conventional.

Many questions remain regarding the potential for infectious disease transmission and the ability to obtain informed consent from third party contacts. As xenotransplantation clinical trials progress, it will be of the utmost importance to monitor the third-party issue closely and create a solution with more specificity. However, because caselaw indicates that it is possible to obtain this higher level of informed consent from the patient through a *Skinner* and *Vernonia* lens, xenotransplantation can and must proceed. Although patients will be subjecting themselves to a life of stricter regulations and medical surveillance, the benefits of xenotransplantation as a life-saving procedure vastly outweigh these infringements. Further, the government has a vested interest in the societal benefit to decrease the immense loss of life from the organ shortage crisis. Therefore, it is in the best interest of society that courts formulate a specific and swift response to the constitutional challenges that arise with xenotransplantation. Ultimately, a dying patient with no other options, along with future patients who will experience the devastating effects of the organ shortage crisis, will have much to gain from the advancement of xenotransplantation.

120. *Id.*