

Of Pigs, PRIMATES and **P**lagues

A Layperson's
Guide to the
Problems With
Animal-to-Human
Organ Transplants

A Report by the
Medical Research Modernization Committee
Alix Fano, M.A.
Murry J. Cohen, M.D.
Marjorie Cramer, M.D., F.A.C.S.
Ray Greek, M.D.
Stephen R. Kaufman, M.D.

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"Seldom, if ever, have we had as much knowledge to prevent a future epidemic. What is lacking is the wisdom to act upon that knowledge."

-Jonathan S. Allan, 'Xenotransplantation at a Crossroads: Prevention Versus Progress,' *Nature Medicine* 2, no. 1 (1996): 20.

I. Introduction

The alleged chronic shortage of human organs has led some researchers and federal health officials in the US and elsewhere to consider using animals such as pigs and nonhuman primates as alternate sources of organs for humans.¹ The prospect of commercial cross-species transplantation or xenotransplantation - which has been attempted since the early 20th century - has created huge financial incentives for biotechnology and pharmaceutical companies.² While some researchers and animal research advocates are optimistic about xenotransplantation's potential,³ others are calling for a moratorium on the technology which, they say, is a threat to public health⁴ and the environment, has an appalling track record, is expensive, and unnecessary.⁵ These concerns have not been satisfactorily addressed by xenotransplantation's proponents, who have overstated the technology's potential benefits to the public. In light of the evidence presented herein, the Medical Research Modernization Committee (MRMC)* advocates a freeze on further xenotransplants.

**The MRMC is a national non-profit organization with about 900 members, over half of whom are physicians and health care professionals.*

The Public Health Risks Posed by Xenotransplantation

- Transplanting living animal organs into humans circumvents the natural barriers (such as skin and gastrointestinal tract) that prevent infection, thereby facilitating the transmission of infectious diseases from animals to humans.
- Many viruses, as innocuous as the common cold or as lethal as Ebola, can be transmitted via a mere cough or sneeze. An animal virus residing in a xenograft recipient could become airborne, infecting scores of people, and causing a potentially deadly viral epidemic of global proportions akin to HIV or worse.
- Viruses that are harmless to their animal hosts, can be deadly when transmitted to humans. For example, Macaque herpes is harmless to Macaque monkeys, but lethal to humans.
- There is no way to screen for viruses that are not yet known. Proceeding with xenotransplantation could expose patients and non-patients to a host of new animal viruses which could remain dormant for months or years before being detected. Xenotransplantation could thus be viewed as a form of involuntary human experimentation which violates US laws and United Nations charters.
- Xenotransplant proponents claim that they will breed "germ-free" animals, thereby diminishing the risk of viral transmission. But it is impossible to breed "germ-free" animals since no animal can remain completely free of parasites or endogenous viruses. In fact, genetically engineered animals are more susceptible to a host of diseases because of weaker immune systems.
- Breeding animals for xenotransplantation would create a host of environmental problems (including soil and groundwater contamination) associated with the disposal of animal waste, and the carcasses of genetically modified animals and their offspring. Conventional farming and rendering operations have yet to solve these problems which continue to threaten public health across the US.
- Proposed regulatory oversight of xenotransplantation procedures is weak and would likely be highly flawed. In all areas of human activity, particularly where there is money to be made, the potential for error, negligence, and fraud exists. Several noted cases of individual and institutional malfeasance described herein demonstrate that such behavior has placed human health at risk before.

Of Pigs, Primates, and Plagues

On March 1, 1997 British researchers reported that pig retroviruses (PERVs)⁶ infected human kidney cells *in vitro* and replicated themselves until the viral particles "were no longer susceptible to destruction by the [human] immune system."⁷ Retroviruses are life-long infections and many are easily transmissible through blood or sexual contact.⁸ Assuming that the numerous problems associated with cellular and vascular rejection were overcome and xenograft recipients survived a xenotransplantation, they could become viral timebombs with the ability to transmit infectious retroviruses to other people. Would public health agencies knowingly expose citizens to such dangers by allowing xenotransplants to be performed?

On September 23, 1996, the US Department of Health and Human Services (HHS) published a set of 'Draft Guidelines on Infectious Disease Issues in Xenotransplantation' in the Federal Register (Vol.61, No.185, pp.49920 - 49932). While the risks posed by xenotransplantation were explicitly acknowledged in the guidelines, the HHS nevertheless appeared to endorse the technology.

On December 20, 1996, the MRMC submitted a 21-page critique of the HHS's draft guidelines, citing 1) epidemiological and public health risks, 2) medical and scientific shortcomings, 3) concerns that xenotransplantation would diminish the importance of preventive health programs and personal responsibility for health, and that it would 4) consume already scarce resources that should be allocated towards practical, safe, and cost-effective health maintenance measures.

Added to this are other concerns including: 1) the enormous investment biotechnology and pharmaceutical companies have made in xenotransplantation, and the tremendous influence such entities exert over federal health authorities, enabling private corporate interests to prevail over public health concerns. (Such was the case with Monsanto's recombinant bovine growth hormone (rBGH) which gained FDA approval despite overwhelming public opposition to the product being forced on consumers, particularly without appropriate labeling). 2) The disturbing genetic reconstruction of life (in this case, the creation of transgenic animals) which is advancing on a commercial scale with almost no informed public discussion or effective oversight. Previous transgenic pig research programs have produced animals with various painful physical abnormalities including arthritis, stomach ulcers, muscular weakness, defective vision, and weakened immunity. Transgenic animals are destined to spend their lives confined in unnatural, sterile environments, unable to fulfill their basic behavioral needs, until death.⁹ 3) The environmental problems posed by the disposal of tens or hundreds of thousands of genetically altered animal carcasses has not been addressed, either in the HHS guidelines, or by the federal government on a national scale. The dumping of tens of millions of gallons of animal waste into the environment each year by traditional hog farming operations has created ideal breeding conditions for deadly microorganisms like *Pfiesteria piscida* which has killed billions of fish, poisoned water systems, and made people sick.¹⁰ The disposal of animal renderings has been recognized as a major problem in traditional farm animal breeding operations.¹¹

The MRMC believes that the HHS draft guidelines on xenotransplantation are woefully

inadequate for several reasons which will be discussed below.

II. Epidemiological and Public Health Concerns:

The HHS guidelines on xenotransplantation provide few real safeguards against the introduction and spread of new infectious diseases in the human population.

The HHS repeatedly raises concerns about infectious disease risks associated with xenograft procedures throughout its draft guidelines. There are several points to be made in this regard. First, it is only possible to test for already identified viruses. All animals have many, perhaps thousands, of viruses within their DNA that remain inactive but could break free by recombination or other means at any time. Second, a zoonotic virus may mutate inside its human host, or recombine with human viral elements, creating new viruses that could be highly lethal.¹² Many viruses (such as HIV) have long incubation periods, often resulting in a manifestation of illness years after an initial exposure.

By the time a new virus was finally identified, it could be too late; a new disease may have already begun to spread among the human population. Third, viruses have different disease presentations in humans and animals; an animal host may live perfectly well with a species-specific virus that is deadly to humans. For example, Macaque herpes is harmless to Macaques, but lethal to humans.¹³ And finally, unlike animal-derived biologic products like porcine heart valves which are treated with glutaraldehyde¹⁴ (and are, according to some physicians, inferior to their synthetic counterparts),¹⁵ implanting living non-human animal organs directly into humans facilitates the transmission of potentially deadly infectious animal diseases to the human population.¹⁶

The HHS itself admits (in paragraph 1.1 of its guidelines) that "public health concerns exist regarding the potential transmission of xenogeneic infectious agents not recognized as classical zoonoses from xenografts to recipients, and then from the recipient to other persons." Moreover "the intimate contact between the recipient and the xenograft, the associated disruption of anatomical barriers, and immunosuppression of the recipient are more likely to facilitate interspecies transmission of xenogeneic infectious agents than normal contact between humans and animals," a concern echoed by respected immunologists and virologists in the UK.¹⁷

Jonathan Allan, a prominent virologist in the Department of Virology and Immunology at the Southwest Foundation for Biomedical Research in San Antonio, Texas, writes that transplantation of animal organs into humans circumvents the natural barriers (skin, mucosal surfaces and the acid environment of the stomach) that prevent infection by these microorganisms, "which means that viruses not typically thought to be infectious for humans such as blood-borne or sexually transmitted pathogens would now have access to human organ systems."¹⁸ Many kinds of cells behave unnaturally when torn from their familiar surroundings. Because cells from transplanted animal organs migrate in the human body, attempt to adapt to their new environment, and integrate themselves inside human cells, a virus that was transmitted from baboons or pigs to humans, could permanently incorporate itself into human chromosomes. Such a virus would remain in the human body even if the animal organ were subsequently removed, as in the case of "bridge organs."¹⁹

In addition, the guidelines assume (paragraph 2.5.3) that zoonotic diseases would only be spread through

sexual contact or the sharing of body fluids. But government scientists admit that many viruses can spread via a mere cough or sneeze.²⁰

The HHS guidelines are voluntary and may be ignored.²¹ Furthermore, they inappropriately leave oversight to surgeons and local review boards rather than federal health authorities, and set the stage for unleashing diseases on the human population, with unknown consequences. In 1996, Jonathan Allan stated that "[the HHS] guidelines provide few real safeguards against the introduction and spread of new infectious diseases in the human population."²² He said, "... lax guidelines in place in the United States will, in effect, jeopardize the health of individuals not only in the US but also globally as we have seen with the rapid worldwide spread of HIV-1."²³ In 1997 Allan reiterated his concerns in light of new findings about pig retroviruses' ability to infect human cells. He said public health officials "should resist the transplant community's clamour for animal organs in light of this new data. Our first priority must be to protect the public health."²⁴

Although the HHS presents a detailed array of precautions, including health surveillance plans, human and animal screening programs, and national registries designed to "minimize" and "diminish" the risk of zoonotic disease transmission, these precautions cannot guarantee negligible risk, which should be an absolute requirement for xenotransplantation.

We Should Learn From the Past

While the HHS reports (p.49920) that live animal cells, tissues and organs are being used in a number of "experimental clinical procedures," they downplay the extremely dangerous nature of such procedures whose clinical value is still unproven.

There are a multitude of scientific unknowns with respect to the existence and behavior of zoonotic viruses. Responsible health authorities would steer clear of xenotransplantation in the interest of human health, particularly in light of the knowledge that animal viruses can jump the species barrier and kill humans. HIV - the virus that causes AIDS, may be a simian immunodeficiency virus (SIV) that leapt the species barrier in central Africa. Health authorities were unable to prevent the worldwide spread of HIV infection. Similarly, they were unable to prevent Ebola outbreaks in Sudan, Zaire (1976, 1979, 1995) and the US (1989, 1996).²⁵ Furthermore, there is evidence that humans have become ill after consuming or being injected with animal materials. There is a reported link between the smallpox vaccine (which used animal cells) and AIDS,²⁶ a recently acknowledged link between human lung, brain and bone cancer and the SV (simian virus) 40 (found in old batches of the Salk polio vaccine),²⁷ and the threat of emerging infectious diseases²⁸ such as human Creutzfeldt-Jakob Disease (CJD) from the consumption of "mad cows" in Europe, the Netherlands, and the US.

Baboon viruses have been found to flourish on human tissue cultures in the laboratory - before killing the cultures.²⁹ Given the acknowledged danger from monkey viruses,³⁰ pigs are being considered as the choice donor animals for xenotransplants. However, pig retroviruses' ability to infect human kidney cells *in vitro* has recently been demonstrated.³¹ Virologists note that the "biologic and pathogenic features of a type C retrovirus" identified in the blood of pigs used in laboratories have not been adequately studied.³² The deadly human influenza virus of 1918 that killed more than 20 million people worldwide was a mutation of a swine

flu that evolved from American pigs and was spread around the world by US troops mobilized for World War I.³³ Leptospirosis (which produces liver and kidney damage), erysipelas (a skin infection),³⁴ and wabah babi, recently discovered in Indonesia,³⁵ are among the approximately 25 known diseases that can be acquired from pigs, (see attached list) all of which could easily be passed onto immunosuppressed humans. There may be myriad unknown "pig diseases" like wabah babi still to be discovered.

Frederick Murphy, Dean and Professor of Virology at the University of California, Davis's School of Veterinary Medicine, reports in the journal *Science* (1996) that "known pathogenic viruses that might pose a risk in xenotransplantation include many adenoviruses, papovaviruses, papillomaviruses, parvoviruses, hepadnaviruses, morbilliviruses, filoviruses, hantaviruses, arenaviruses, arteriviruses, flaviviruses, and togaviruses . . . certain retroviruses (including endogenous retroviruses, mammalian type C and D retroviruses, lentiviruses, and human T cell leukemia virus/bovine leukemia virus-like viruses) and certain animal herpesviruses (including herpes simplex-like viruses, Epstein-Barr-like viruses, cytomegaloviruses, and HHV6-, 7-, and 8-like viruses) must be considered further."³⁶ This is alarming, and it is highly unlikely that the HHS guidelines could prepare scientists and health care workers to cope with such a lengthy list of known dangers.

How Would Our Health Care System Cope With the Consequences of Infection?

Although the HHS acknowledges the risks of spreading xenogeneic viruses to the human population, it does not examine the long-term implications of unleashing such viruses on society.

Prominent virologists note, and history has taught us, that it is easier to prevent a viral epidemic than to contain one. Containment, screening and treatment are extremely costly for governments; treatments are not always successful and cures are rare. Should a xenogeneic agent be discovered at a later date, it could be virtually impossible (as it was during the AIDS crisis) to locate all infected individuals, or those who may have had contact with infected individuals. More importantly, it may be impossible to determine the original source of infection. The HHS concurs that "most acute viral infectious episodes among the general population are never etiologically identified" (paragraph 4.3.2).

Several questions therefore arise and they have yet to be adequately addressed:

1. How would federal agencies identify carriers of the virus in the general population once the virus was dispersed?

It is naive to believe that the creation of a national registry/database to assess the long-term safety of xenotransplants and the health of xenograft recipients would be adequate to track the progress of a retrovirus, particularly one that is not known. The Vaccine Adverse Event Reporting System (VAERS), for example, established in 1990 and managed by the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) has been described by epidemiologists at the FDA and CDC as "a reporting system . . . [with] . . . major limitations, including under-reporting, lack of specificity, and a lack of a natural control group." The lack of enforcement or monitoring of reporting practices leads to serious inconsistencies in the data that are collected.³⁷ The VAERS database is a repository for voluntarily submitted reports, but are there any guarantees that a mandatory reporting system would work?

Given the enormous amount of data, paperwork, and filing xenotransplant procedures would generate, it would be naive to assume that human error or negligence won't come into play somewhere along the line in the form of a miscalculation of numbers, misinterpretation of data, misfiling of folders, improper labeling of files or slides, and so on. A San Diego-based food company was recently blamed for mislabeling imported strawberries and shipping them to public schools in seventeen states, resulting in almost 200 cases of hepatitis A, with thousands more possibly affected.³⁸ The Federal Bureau of Investigation's crime laboratory was recently criticized for submitting flawed scientific findings in at least 55 cases. A report found that scientific examiners (including chemists and toxicologists) had prepared "sloppy reports, exaggerated their findings . . . and inadequately documented their test results." Supervisors had left too much discretion to subordinates "who reached findings that were unsupportable by scientific evidence." Moreover, laboratory managers had failed to respond to internal complaints.³⁹ These cases illustrate that error and negligence are an inevitable part of human activity. Regulatory mechanisms often fail to prevent or correct these errors and/or behaviors, the consequences of which could be disastrous in the face of a xenogeneic infection.

2. How would federal agencies contain an infectious epidemic caused by an unfamiliar xenogeneic agent, particularly when US doctors are currently not required to report cases of Ebola, nor any other disease they cannot identify, to the CDC?⁴⁰

The AIDS Action Council in Washington, DC issued a report in 1991 entitled *Good Intentions* which evaluated early HIV prevention efforts in the US; the Council found "poor federal inter-agency coordination,"

poor long-term planning, and insensitivity to women and people of color.

If carriers of a zoonotic virus were identified, would they all be quarantined/placed in isolation? What if there were thousands or tens of thousands of carriers? Would special

facilities have to be built to accommodate them? If so, who would pay to build these facilities?

3. *How would research centers identify unknown and unidentifiable microbes or illnesses?*

In 1992, there were 744 unexplained deaths

attributed to infections in four states across the US.⁴¹ Robert Michler, Director of heart transplant service at New York's Columbia-Presbyterian Medical Center admits that "it is difficult to monitor for the unknown."⁴² As Jonathan Allan writes, "there is no way to screen for viruses that have yet to be discovered . . . (and there may be several of these)."⁴³

CDC officials have estimated that before Legionnaire's diseases was identified in 1976, 2,000 - 6,000 deaths per year were incorrectly attributed to pneumonia. Similarly, although the HIV virus was identified in 1983, researchers have now discovered cases that may date as far back as 1968.

The CDC's Unexplained Illnesses and Deaths Surveillance project was established in 1994 in an attempt to combat emerging infections. The project's two dozen researchers have only been able to explain about 10% of the cases they have reviewed.⁴⁴ Failure to identify an emerging zoonotic infection could be catastrophic.

4. *Who would pay to develop appropriate screening assays and screening programs for a new virus (assuming one could be developed quickly enough)?*

The US military spent \$43 million between 1986 and 1988 screening 3.2 million new volunteers and existing personnel for HIV.⁴⁵ It should be noted that diagnostic, sampling and analytical technologies and equipment are fallible.⁴⁶ Assays may fail to detect an infection in an individual, a hospital, or a blood center's blood supply, or they may falsely detect infection where none exists. The HHS admits that "immunosuppressed transplant patients may be unable to mount a sufficient immunological response for serological assays to detect infections reliably" (paragraph 4.3.2.1). Jonathan Allan points out that the assays used to detect infection in animals, particularly primates, have not been assessed for their specificity or sensitivity.⁴⁷ This suggests that a new zoonotic virus may not be detectable in the xenograft recipient until it is too late, and a new disease may have begun to spread. In addition, physicians and/or laboratory personnel may misread or misunderstand lab results. A recently published report in *The New England Journal of Medicine* revealed that nearly one-third of physicians who referred patients for tests to detect genetic mutations misinterpreted the test results. More importantly, about 32% misunderstood the meaning of a negative result.⁴⁸ Failure to identify genetic mutations or other cellular abnormalities in xenograft recipients' test results could lead to another public health crisis akin to AIDS or Ebola.

5. *Assuming all of the xenograft recipient's contacts (paragraph 2.4), could be located and identified, and assuming assays gave reliable results and were interpreted correctly, who would pay to screen all of these individuals, presuming they agreed to submit to testing? If they did not agree to testing, would they be forced to submit to it?*

Experience with HIV has shown that, "where control measures such as mandatory testing are considered by authorities, the level of voluntary requests for testing drops; an atmosphere of coercion has had the effect of frightening people away from testing and treatment centers, driving AIDS underground."⁴⁹

Would individuals' behavior and whereabouts be constantly monitored? In this regard, the guidelines fail to take the basic vicissitudes of human nature into account, particularly with respect to the xenograft recipients themselves. The rigorous and "potentially life-long surveillance" program, requiring complete physical exams and sampling regimens (paragraphs 2.5.5, 4), could backfire. Individuals may tire of such a regimen and secretly relocate, never to be found again. Health care workers are also asked to submit to sampling and surveillance regimens (paragraph 4.3.3.2) which could backfire or be disregarded. Workers who may accidentally prick themselves with an infected needle, for example, (paragraph 4.3.3.3), may not record or report the exposure, or archive it in the 'Health Exposure Log,' for fear of losing their jobs. The implications for public health of this scenario, which would be compounded if these workers changed jobs or moved to another city or state, are obvious.

With respect to carrying out procedures outlined in the guidelines, the guidelines fail to consider that a percentage of laboratory, health care, and surgical personnel may be prone

to laziness, carelessness/sloppiness, fear and outright deceitfulness. Decades of secrecy, mismanagement, and conscious violations of public health and environmental laws by personnel at the Department of Energy's Brookhaven National Laboratory in Long Island were recently brought to light. In May 1997, the Federal Government admitted that "safety had taken a back seat to science" at the Laboratory.⁵⁰ *The New York Times* reported that the Laboratory went about its business "like any other manufacturing site," its workers dumping industrial solvents, low-level radioactive waste and pesticides around its 5,300-acre property, contaminating private water wells and Suffolk County's aquifer - the sole source of drinking water for three million Long Island residents. The additional discovery of leaks of tritium and other radioactive substances from the Laboratory was attributed to 'awry decision-making' according to a DoE official.⁵¹

Other noted examples of institutional malfeasance include the HIV-contaminated blood scandals in France, China and Japan in which medical authorities knowingly allowed HIV-contaminated blood to be used for transfusions and blood-clotting treatments for hemophiliacs.⁵² In the 1980s, the Pennsylvania-based Armour Pharmaceutical Company knowingly continued selling a blood-clotting drug in Canada despite warnings that its heat-treatment process wasn't killing the AIDS virus, causing thousands of Canadians to become infected with AIDS and hepatitis C.⁵³ Similarly, four pharmaceutical companies: Bayer AG (Germany), Baxter International Inc. (Illinois), Rhone-Poulenc Rorer Inc. (France), and Green Cross Corp. (Japan) - infected about 8,000 Americans with HIV in the 1980s through contaminated blood-clotting substances.⁵⁴ A report released by the Institute of Medicine in 1995 found

that the government, manufacturers and the National Hemophilia Foundation all failed to move swiftly to insure the safety of blood-clotting products in the 1980s.⁵⁵ US Food and Drug Administration investigators recently found "continuing violations in blood safety laws and regulations" at the New York Blood Center which supplies 80% of the blood used in New York hospitals. A night shift manager was arrested for "taking short cuts to manipulate the testing of blood for viruses like HIV and hepatitis."⁵⁶ A similar scenario with a zoonotic virus would have unforeseeable public health and economic repercussions.

6. Who would pay for long-term treatment and care of infected individuals?

Current drug therapies for AIDS (protease inhibitor cocktails) cost up to \$20,000 per year.⁵⁷ To treat all 30 million people with AIDS would cost \$6 billion per year.⁵⁸ Add to that fees for hospital stays, doctor visits, and blood tests. The hundreds of millions of federal dollars spent on AIDS research, including \$129 million recently allocated to develop a vaccine,⁵⁹ should also be tallied; such increased spending is an inevitable consequence of an epidemic. Clearly, treating and caring for individuals infected with a new xenogeneic virus would cost the US billions.

7. Because no regulatory system is foolproof, how could public health agencies ensure that xenograft recipients and their families understood, and were adequately informed about, the risks involved in xenotransplantation procedures?

The concept of informed consent was developed after World War II, as a result of Nazi experiments conducted on unwilling human prisoners. Rules were consequently designed that were supposed to protect volunteers and patients in medical research. However, *The New York Times* reported that

consent forms, which must be signed by patients or their relatives, do not always fully explain the risks of experimental procedures. Patients have been permanently damaged or killed by treatments that were supposed to heal them, leading some health experts to express concern about "unchecked human experimentation" taking place in hospitals, universities, and private laboratories throughout the US. Legislators have held hearings "to determine the scope of lapses and violations of ethics in experiments."⁶⁰

Patients undergoing xenotransplantation procedures would have to be informed of the risks to themselves, their families, friends, and society at large. But how would the process of informed consent in xenograft procedures be monitored?

Who would ensure that patients and their families were fully informed of all the risks? What of patients who may choose to participate in privately-funded research where there are no mechanisms of accountability to federal health authorities, and little chance of receiving remuneration for injury or death? Is the field of xenotransplantation immune from "unchecked human experimentation" and "violations of ethics?"

8. A majority of non-smokers feel that their rights and their health⁶¹ are compromised when they are forced to breathe second-hand cigarette smoke. What of the rights of people who may inadvertently come into contact with xenograft recipients harboring potentially pathogenic agents?

"What of patients who may choose to participate in privately-funded research where there are no mechanisms of accountability to federal health authorities, and little chance of receiving remuneration for injury or death?"

While patients may give their consent to undergo xenotransplants, it would be impossible to obtain consent from every person the xenograft recipients may come into contact with (should they survive). This situation raises serious legal questions because it could constitute a form of involuntary human experimentation, in violation of the 1964 UN 'Helsinki Declaration' on Biomedical Research Involving Human Subjects as well as the 1993 International Guidelines for Biomedical Research Involving Human Subjects, the US rules of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, and new rules adopted by the US government to prohibit secret experiments on unwitting human subjects.⁶²

9. Would the US government be prepared to compensate victims of xenogeneic infections (such as people who may have inadvertently contracted an infection from a xenograft recipient)?

HIV-1 and HIV-2, two immunodeficiency viruses linked to monkey viruses, infected more than 12,000 people through blood transfusions before the disease was recognized and discovered.⁶³ The French government was forced to establish a \$2.2 billion fund to compensate victims of AIDS-contaminated blood transfusions administered between 1980 and 1985.⁶⁴ Compensation claims in the US have been filed by Persian Gulf War veterans,⁶⁵ victims of secret government-sanctioned radiation⁶⁶ and syphilis experiments,⁶⁷ Vietnam war veterans exposed to Agent Orange,⁶⁸ and parents of vaccine-damaged children.⁶⁹ The government may now also be held liable for failing to protect citizens from SV (simian virus) 40-contaminated polio vaccine.⁷⁰

In addition, it has been pointed out that the harmful consequences of global

epidemics are almost always more lethal in poor, undernourished communities.⁷¹ Has any thought been given to the ethical and economic ramifications of unleashing a new retroviral illness in developing countries? Can our government afford such a global public health catastrophe?

10. Where would potentially infectious animal tissues be stored? What about power failures? What if computer hackers or intruders were to destroy the health records of all the source animal herds, and/or the clinical data relevant to xenograft recipients?

The Limited Value of Risk Assessment

Although the HHS admits (p.49922) that "the introduction of xenogeneic infectious agents into and propagation through the general human population is a risk that must be addressed," ultimately, writes Frederick Murphy, "risk may be revealed only through ongoing surveillance and clinical observation,"⁷² - in other words, after disaster has already struck, as with the AIDS crisis.

Paragraph 2.3, the 'Clinical Protocol Review,' recommends that local Institutional Review Boards have expertise in risk assessment vis-a-vis the transmission of zoonotic viruses to humans. But risk assessment is a precarious "science" which is often subject to enormous political manipulation. The outcome of most risk assessments depends on a risk assessor's subjective selection and interpretation of data (including statistical analyses). According to David G. Hoel et al., different statistical models can yield risk estimates that vary over a wide range.⁷³ Performing a risk assessment does not reduce the risk of a dangerous occurrence, it is merely an attempt to assess the danger. Ultimately, risk assessment is a hypothesis that can only be tested and validated by the occurrence of the very event one is trying to prevent.⁷⁴

Some risks, such as the disease risk to "health care workers who provide direct/indirect post-transplantation care for xenograft recipients" (paragraph 4.3.3) remain undefined and may be heightened or diminished by the adequacy of "biosafety standards" that are employed. Here again, steps are suggested that may "minimize," rather than eliminate exposure and transmission of zoonotic and nosocomial agents between the (xenograft) recipient(s) and health care workers (paragraph 4.3.3.1). But risk must be negligible when the public health implications are so great.

Animal Viruses and the Myth of the "Germ-Free" Animal

In paragraph 3, the HHS outlines detailed "source animal" breeding, husbandry, and screening protocols designed to "minimize" the risk of transmitting infectious animal diseases to humans. The surveillance programs are to be "adequate" (paragraph 3.4) though the term adequate is not defined anywhere. Not only is the assessment of the "adequacy of the screening program" left to the discretion of the xenotransplant team (for whom objectivity may be difficult), but the precautions are illusory. Indeed, the HHS concedes that the source animals and "all procured cells, tissues and organs intended for clinical use" should be "*as free as possible of infectious agents*" (emphasis added), (paragraphs 3.1.2 and 3.5.2). Moreover, it is recognized that animals may contract diseases during transport. It has also been shown that animals, specifically rodents and rabbits, whose food, water and bedding are sterilized, who live in barren sterile environments in which temperature, humidity, lighting are controlled, and who are kept in isolation/deprived of social interaction, are far more susceptible to immunosuppression and a host of diseases including cancer, than their wild counterparts.⁷⁵ Undoubtedly, that

is why pigs, who are very social, playful, sensitive, and intelligent animals,⁷⁶ possessing IQs surpassing even the dog,⁷⁷ do not thrive in such sterile, artificial environments⁷⁸ - a problem for those who would seek to breed them in large numbers for xenotransplantation. Indeed, of 49 transgenic pigs bred by Imutran, a UK-based biotechnology company, 20% - 25% were either stillborn, died or were killed soon after birth.⁷⁹

A report by the (British) Advisory Group on the Ethics of Xenotransplantation concluded that the risks of animal organs being infected with bacteria, fungi, parasites, and prions were "ethically acceptable" provided that donor animals were bred in specific pathogen free (SPF) environments.⁸⁰ That is an irresponsible statement. Prions - abnormal forms of proteins that enter the brain and force normal proteins to mutate - have been identified as the agents that can cause Creutzfeldt-Jakob disease in humans and bovine spongiform encephalopathy (BSE) in cows. Prions are resistant to boiling, formaldehyde, and ultraviolet and gamma-irradiation, and prion-related diseases remain latent for long periods of time.⁸¹ Prions occur naturally in the brains of all mammals, hence no animal can be free of them.⁸²

In fact, no animal, whether transgenic or otherwise, can remain completely free of parasites or endogenous viruses. Clive Patience et al. say, for example, that it would be "a daunting task to eliminate infectious retroviruses from pigs to be used for xenotransplantation, given that [they] estimate approximately 50 PERV [pig endogenous retroviruses] per pig genome."⁸³ In its June 1996 report, the Institute of Medicine acknowledged that "it is not possible to have completely pathogen-free animals, even those derived by Cesarean section, because some potentially infectious agents are passed in the

genome and others may be passed transplacentally." Even Charles River Laboratories, (which breeds animals for laboratories) in Wilmington, Massachusetts, admits that potentially pathogenic organisms are difficult to exclude in specially bred animals "without extraordinary measures." The company recommends a detailed health monitoring and diagnostic evaluation program which requires the expertise of parasitologists, microbiologists, pathologists and serologists. Charles River acknowledges that labs must select the agents for which they wish to screen due to the "prevalence of agents" and the "cost of screening."⁸⁴ Indeed, who would pay for these elaborate and extremely costly animal breeding, "life-long monitoring" and tissue and data archiving programs (see paragraph 3.4 - 3.7.4)?

The HHS states that extensive screening of the source animal(s) may sometimes be limited "to ensure graft viability," (paragraph 3) and that imported animals and their offspring may be used if the animals belong to "a species or strain not available for use in the United States" (paragraph 3.1.5). However, importing monkeys, for example, into the United States for biomedical research has placed the safety of Americans in jeopardy before, exposing them to the deadly Ebola-Reston, Marburg and herpes B viruses. Monkey STLV may have resulted in cross-species HTLV-2, which causes human leukemia; and the hepatitis B virus may have originated from human exposure to asymptomatic chimpanzee carriers.⁸⁵ Hence the practice of importing animals from other countries for medical purposes should be stopped in the interest of public health.

In paragraph 3.3, the HHS recommends a "characterization of the human pathogenicity of xenotropic endogenous retroviruses and persistent viral infections present in source

animal cells, tissues, and organs." This is feasible for *known* infectious agents, but as was previously pointed out, there is no way to screen for viruses that have yet to be discovered.

The HHS also states that "the use of live vaccines . . . may be justified when dead or acellular vaccines are not available" (paragraph 3.4.1, 3.5). As discussed, live vaccines are a public health concern because they can contain potentially deadly infectious agents. The clinical impact of administering live vaccines to "source animals" whose organs may then be transplanted into humans, can never be assessed in advance.

Scientists have recently reported that the accidental transmission of Creutzfeldt-Jakob Disease (CJD) to patients, transplant surgeons, and histopathology technicians is becoming more common "in the high-technology milieu of modern medicine."⁸⁶ Given the health threat posed by bovine spongiform encephalopathy (BSE) (which causes human CJD),⁸⁷ it is irresponsible for the HHS to suggest that bovine tissue be used for transplantation (paragraph 3.1.6), despite the warning that such tissues not be obtained from countries where BSE exists. First, CJD is making unannounced appearances in the US, the UK, France, Italy,⁸⁸ and the Netherlands,⁸⁹ and it is unknown how many citizens in other countries may be harboring the illness.

It is unknown how many countries monitor their herds for BSE, and how many would admit to having the problem, particularly if such an announcement would result in the compulsory destruction of entire cow herds, thereby incurring large economic losses.⁹⁰ Britain, for example, has been eager to proclaim that its cow herds are healthy; but reductions in

"no animal, whether transgenic or otherwise, can remain completely free of parasites or endogenous viruses."

compensation payments for infected cattle in Britain resulted in fewer farmers reporting cases of BSE and then sending diseased cattle to market, rather than risk losing money by reporting them to the Ministry of Agriculture.⁹¹ In March 1997 the British Government was accused of suppressing a year-old report that found slaughterhouses guilty of practices that could contribute to the spread of mad cow disease.⁹² According to *The Economist*, the study of BSE “has been hobbled by secrecy and government bungling.” Basic questions about how the disease is transmitted remain unanswered.⁹³

When the Foxes Guard the Henhouse

It should be noted, and the HHS readily admits (p.49921), that all animal-to-human transplants executed prior to 1996 were performed without the existence of guidelines regarding the “adequate screening of donor animal cells, tissues, and organs intended for human transplant or recommendations for post-transplantation patient monitoring.” There was also no federal oversight, with research centers being left to their own devices. Xenograft researchers have opposed federal oversight. For example, Suzanne Ildstad⁹⁴ praised the FDA for drafting (unenforceable) guidelines, as opposed to legislation, for the research.⁹⁵

The current climate of deregulation in biotechnology favors the unhindered continuation of xenotransplantation research, despite the risks to human health. Jonathan Allan writes that, “in choosing voluntary guidelines to be enforced at a local level, rather than federal regulations, the FDA/CDC committee has chosen the least stringent and possibly least successful method of policing these transplant procedures.”⁹⁶ Oversight of the entire xenotransplant operation and its aftermath would be left to the

discretion of local review boards, surgical staff, and health care workers. But *The New York Times* reported that legislators have been “startled” by accounts of “ethics panels, institutional review boards, [IRBs] . . . set up as profit-making ventures to evaluate proposed experiments for research groups that pay them.” Researchers, particularly those receiving money from private industry, allegedly “shop” for IRBs that will approve their research.⁹⁷

Although the HHS has proposed allowing local IRBs to oversee xenotransplantation procedures, federal health authorities would be called upon to respond to a potential public health disaster resulting from the procedures (paragraph 4.1.1.6). These authorities will, until that point, have been completely out of the loop with respect to the facts, methods, and risks involved in the xenotransplantation(s). From a public health and public policy standpoint, the MRMC believes that this scenario is unacceptable.

In summary, the HHS recognizes the risk of unleashing a viral epidemic upon society through acknowledging that: an infectious agent may be identified in the source animal or herd “subsequent to xenograft harvest” (paragraph 3.5.5); that “necropsy findings [may] reveal infections pertinent to the xenograft recipient” (paragraph 3.6.5); that archived source animal biologic samples are essential for public health investigation and “containment of emergent xenogeneic infections” (paragraph 3.7); that “post-transplantation clinical and laboratory surveillance of xenograft recipients is critical to monitor for the introduction and propagation of xenogeneic and infectious agents in the general population” (paragraph 4.1.1); that biological specimens of xenograft recipients should be collected and archived to allow “retrospective

investigation of possible xenogeneic infections” (paragraphs 4.1.1.2, 4.3.2.2), and to detect “sentinel human infections prior to dissemination in the general population” (paragraph 4.1.1.5). We do not share the HHS’s view that these risks are acceptable.

III. Medical and Scientific Concerns:

Xenotransplantation is biologically irrational because it falsely assumes that human and non-human body parts are interchangeable. The dismal track record of previous animal-to-human organ transplant attempts is being ignored by the technology’s proponents. Animal-to-human transplants have been deadly in some 55 recipients and ineffectual in one (Jeff Getty). The technology is dangerous and unproven.

Xenotransplantation is Dangerous and Unproven

The HHS states (p.49920) that “xenotransplantation shows promise for a wide range of diseases . . . and as an alternative source of cells, tissues and organs for clinical transplantations.” This statement is powerfully contradicted by clinical evidence. In fact, the history of basic animal research, and extremely limited clinical research with humans in the field of xenotransplantation, has been marred by failure.

Alexis Carrel, the French surgeon who had transplanted organs, and grafted veins and skin between dogs, cats and monkeys in the early 1900s, discouraged other surgeons from trying the experiments because his had all failed. Arthur Caplan, professor of bioethics and Director of the Center for Bioethics at the University of Pennsylvania School of Medicine has said, “there’s absolutely no basis in basic research for trying a pig liver in a human being given the differences in biology between people and pigs.”⁹⁸ Similarly, in 1984, Jacques Losman, a

cardiac surgeon from the Beth Israel Hospital in Newark, who had worked with Christian Barnard's heart transplant team in South Africa said, "all animal experiments have shown that transplants from one species to another fail . . . I don't think there was much scientific basis to believe that this would work."⁹⁹

There have been some 55 documented animal-to-human whole organ transplants since 1906.¹⁰⁰ All have proven unsuccessful. For example:

- In 1906, a French surgeon, Mathieu Jaboulay, joined a pig kidney to a patient's left arm. The organ turned black and blue and had to be removed after three days. He tried using a goat's kidney several months later to no avail.¹⁰¹
- In 1909, Ernest Unger, a surgeon from Berlin, transplanted the kidneys of a Macaque monkey into a 21-year-old woman's left leg. She died thirty two hours later.¹⁰²
- In 1923, Harold Neuhof, an American, transplanted a kidney from a lamb into a human who died nine days later.¹⁰³
- In 1963, Claude Hitchcock, a surgeon at Hennepin County Hospital in Minneapolis, transplanted a baboon's kidney into a sixty-five-year-old woman. After four days, the baboon organ's main artery clotted and the transplant failed.¹⁰⁴
- In 1963 and 1964, Keith Reemstma performed chimpanzee-to-human kidney transplants in 12 adults at Tulane University. All the human patients died within a few weeks of their operations. One recipient survived for nine months before dying of an infection. Subsequent attempts to transplant a chimpanzee heart and kidney failed.¹⁰⁵
- In 1963, Claude Hitchcock and Thomas Starzl transplanted 6 baboon kidneys into 6 human adults. The patients survived from 19 to 98 days. In 1966, 1969 and 1973, Starzl transplanted chimpanzee livers into three children. None survived longer than 14 days.¹⁰⁶
- In 1964, Raffaello Cortesini, an Italian surgeon transplanted a chimpanzee kidney into a nineteen-year-old male who died thirty days later. The chimp died after two years. Cortesini performed other chimp transplants in the 1960s.¹⁰⁷
- In 1964, James Hardy, an American cardiac surgeon transplanted a chimpanzee heart into a sixty-eight-year-old man who died two hours later. The chimpanzee heart proved too small to support the patient's circulation.¹⁰⁸
- In 1968, Denton Cooley, a cardiac surgeon in Texas, and his colleague D. N. Ross, transplanted sheep and pig hearts into dying human recipients. The patients died, one right on the operating table.¹⁰⁹
- In 1977, Christian Barnard transplanted a chimpanzee heart into a 26-year-old woman whose own sick heart was left inside her body. She died six hours later. His second patient, a 59-year-old man, died after four days.¹¹⁰
- In 1984 Leonard Bailey transplanted a baboon heart into new-born "Baby-Fae" at Loma Linda University. The baby died 20 days later because her arteries and veins became blocked - a response to the baboon blood in her body. No attempt was made to find a human heart, though one might have been available.¹¹¹ The experiment was condemned by Bailey's peers and by the media, leading to an unofficial moratorium on xenotransplantation.
- In June 1992 at the University of Pittsburgh, a 35-year-old HIV positive man with hepatitis B died 70 days after receiving a baboon's liver. (Baboons are often infected with Cytomegalovirus, Epstein-Barr, and other viruses). Before dying, the patient developed several infections, including Cytomegalovirus, *Candida* esophagitis, *Staphylococcus aureus*, *Enterococcus faecalis*, *aspergillus*, and duodenitis which caused recurrent gastrointestinal hemorrhages over a two-week period. Other complications included renal and liver failure, toxicity from elevated doses of immuno-suppressive drugs, viraemia, blood pressure and circulatory collapse, and bile engorgement. The patient had to have several blood transfusions and had to be intubated before he suffered a brain hemorrhage and died. At autopsy, it was discovered that baboon cells had migrated in his body and lodged themselves in his skin, nose, heart, and other vital organs.¹¹² Virologist Jonathan Allan has stated that, "retroviruses pose a serious problem because of their inherent ability to integrate into human chromosomes with the potential for inducing cancer."¹¹³
- In June 1992, at the Cedars-Sinai Medical Center in Los Angeles, surgeons implanted a conventional pig's liver into a 26-year-old woman as a "bridge" until a human liver could be found. The woman died in 30 hours, two hours before a human liver was flown in from Utah.¹¹⁴ That year, Czaplicki et al. transplanted a pig heart into a human with Marfan's syndrome; the recipient died in less than 24 hours.¹¹⁵
- In January 1993, a 62-year-old hepatitis B patient received a baboon liver transplant at the University of Pittsburgh in a 13 1/2 hour operation. He never regained consciousness and died 26 days later of an infection of the membrane covering his intestines. At other centers, hepatitis B patients have been successfully treated with human liver transplants.¹¹⁶
- In December 1995, an AIDS patient in San Francisco received a baboon bone marrow transplant in the hope that the baboon cells would help the patient's immune system become resistant to HIV. The patient received chemotherapy, radiation, antibiotics and doses of immuno-suppressive drugs. On February 8, 1996, *The New York Times*, *USA Today*, and *The Newark Star-Ledger* all reported that the baboon bone marrow had failed to boost the patient's immune system. That was reconfirmed by *The New York Times* on December 16, 1996, p.A12. The danger of the patient transferring dangerous microorganisms to other humans has not been adequately assessed.

"A pig heart put into a human will turn black and stop beating in about fifteen minutes and there is no evidence that this acute cellular and vascular rejection will ever be overcome."

- In December 1995, a 32-year-old Indian man died soon after a pig heart transplant. The surgeon, Dhaniram Baruah, was jailed for violating the Organ Transplant Act of 1994 following

complaints from the victim's family that the death took place under mysterious circumstances.¹¹⁷

Animal experiments have been equally unsuccessful. For example:

- In the 1950s, the English surgeon Roy Calne transplanted organs between dogs and used dogs and rabbits to experiment with immunosuppressive drugs.¹¹⁸
- From 1959, Norman Shumway, a cardiac surgeon in California, transplanted hearts between dogs. A decade later, Shumway was eager to try his experiments on humans acknowledging that, "survival of dogs after any kind of cardiac surgery is different from people."¹¹⁹
- In the 1960s, James Hardy transplanted hearts and lungs between dogs at the University of Mississippi Medical Center in Jackson. All the animals died within a month of their surgeries.¹²⁰
- By 1967, Christian Barnard and his surgical team had performed about 50 cross-species transplants between dogs and other animals, without immunosuppressive drugs.¹²¹ All the animals died soon after their surgeries.
- By 1979, Leonard Bailey had performed about 100 goat-to-goat organ transplants; by 1984 he had completed circa 160 cross-species transplants, grafting hearts from lambs and piglets into young goats. None of the animals survived longer than six months.¹²²
- In the 1970s and 1980s, Robert White performed up to thirty *head* transplants between monkeys. Once rejection took its toll, the monkeys' faces started to swell and bleed. All died within a week. White hopes to go to the Ukraine, where

restrictions on medical research are less stringent, to try his head/whole body transplants on humans.¹²³

- In 1992 at Ohio State University College of Medicine, pig kidneys were transplanted into the necks of at least 15 mongrel dogs. The grafts all failed within a few hours.¹²⁴
- In 1992, at Milan University in Italy, 19 pigs underwent transplant operations in which they received sheep livers. In 1993, an Italian researcher attempted to transplant rats' hearts into chickens. All the animals died within hours.¹²⁵
- In 1993 at the University of Minnesota Hospital and Clinic in Minneapolis, 5 baboons received pig hearts. The last survivor died after 92 hours.¹²⁶
- In April 1995, in New York, researchers at Alexion Pharmaceuticals transplanted transgenic pig liver and lungs into three baboons and withheld immunosuppressive drugs. The baboons died after two days.¹²⁷
- Scientists at Imutran, Ltd. in Cambridge, UK have transplanted rabbits' hearts into the necks of 17 new-born pigs. In order to observe the results, the wounds were left open and covered with plastic film.¹²⁸ In April 1996, *The Times* of London reported that in 1995, Imutran, Ltd. researchers transplanted 18 transgenic pig hearts into monkeys, none of which survived longer than 60 days.¹²⁹ Monkeys who had pig hearts transplanted into their abdomens died after five and a half days.¹³⁰
- David H. Sachs, at Harvard University Medical School is also conducting pig-to-monkey transplants.¹³¹

Though similar animal experiments are being conducted in universities and research centers across the country, they cannot provide reliable information about what would happen to human xenograft recipients. As it stands, animals who receive transplanted organs from other species (rats-to-hamsters, pigs-to-primates, cats-to-dogs, and so on) have poor survival rates that do not correlate

with human allotransplant survival patterns. Xenografted organs are hyperacutely rejected within minutes, hours, or days.¹³² Animals often die from complications such as infections.¹³³ Immunosuppressive drugs have not significantly increased survival rates.¹³⁴ In addition, results of animal experiments with immunosuppressive (and other) drugs vary widely because of differences in species' metabolism.¹³⁵ An article in the FDA publication, *MedWatch*, revealed that "Animal studies have limitations in their ability to predict human toxicity," citing examples of numerous drugs whose side-effects were not predicted in animal tests.¹³⁶ David J. Cohen, et al. note that "oral administration [of cyclosporine] in humans results in highly variable rates and degrees of absorption."¹³⁷ That is perhaps why animal experiments with cyclosporine and other anti-rejection drugs did not predict their side-effects in humans¹³⁸ and misled surgeons about the correct dosages for human transplant patients.¹³⁹ Ultimately, human beings are the only reliable experimental subjects, because animal models cannot mimic the human condition.

Researchers have suggested performing xenotransplants on chronically ill patients, on infants and children without access to mechanical assist devices, on "large" (or overweight) patients with type O blood, and on patients with conditions which make them ineligible for allotransplants.¹⁴⁰ As in the majority of earlier xenograft cases, this appears to be a select group of patients with little hope of survival to begin with. Should our society condone this kind of human experimentation, the "premature use of unproven procedures in fellow humans,"¹⁴¹ before exploring safer alternatives?

Robert Michler, of New York's Columbia-Presbyterian Medical Center suggests that, as was the case with allotransplantation, the clinical

'success' of xenotransplantation could be measured in terms of short-term survival rates, with the goal to strive for "extended graft survival."¹⁴² In other words, if a xenograft recipient survives for ten days with a pig organ, that operation could be deemed a "success." Is that an acceptable standard for such a dangerous and expensive technology? Ultimately, it is the public, not a select group of research scientists, or pharmaceutical or biotechnology executives, who must answer such questions.

Pigs Vs. Baboons: Logic or Convenience?

The notion that pigs, because of their genetic dissimilarity to humans, could provide a safer source of tissues and organs for xenotransplantation than primates, for example,¹⁴³ is erroneous and has been discredited by the incidents of malaria, Dengue and yellow fever (from mosquitoes), Lyme disease (from ticks), rabies (from dogs, raccoons), human brucellosis (from cows, sheep, goats, pigs), bubonic plague, and the 50% human mortality rates associated with hantavirus pulmonary syndrome (from rodents).¹⁴⁴ Moreover, pigs' genetic dissimilarity to humans raises important questions. Ethical issues and disease risks have virtually precluded the use of chimpanzees and other great apes as organ donors. Are pigs the next best thing for those determined to implement the technology, or is there truly a scientific rationale for using pigs? The fact that they breed quickly, or have been "extensively farmed," or have organs that are "similar" in size to ours,¹⁴⁵ does not qualify as scientific justification for their use.

It has been suggested that pigs are anatomically and physiologically "similar" to humans.¹⁴⁶ But there are differences in life-span, heart rate, blood pressure, and the structure of the regulatory hormones which maintain the basic physiological stability of the animal.¹⁴⁷ The author of

an article in *Nursing Times* asks, "Can a pig's heart - normally on the same level as its head - pump enough blood to a human brain 15 - 18 inches above? Will a pig kidney filter human blood effectively, or will the pig's different uric acid metabolism lead to biochemical aberrations? And will the human recipient's immune system work in a transplanted pig organ?..."¹⁴⁸ A pig heart put into a human will turn black and stop beating in about fifteen minutes¹⁴⁹ and there is no evidence that this acute cellular and vascular rejection will ever be overcome.

Nor is there any clinical evidence to suggest that organs from genetically bred pigs are any less likely to be rejected by the human body than those from conventional pigs. The massive doses of immunosuppressive drugs that would be required for such an operation would likely cause toxicity, increase the patient's chances of developing cancer,¹⁵⁰ and, as discussed, would likely facilitate the transmission of a xenogeneic virus from the animal to the patient.¹⁵¹ Scientists from the FDA and the CDC have also pointed out that "the short life expectancy of the average pig minimizes the opportunity to observe the clinical manifestations of infections with agents that have long periods of clinical latency."¹⁵²

Xenotransplantation remains an unproven, highly experimental, and potentially virulent procedure.

IV. The Power and Wisdom of Prevention:

Emphasizing xenotransplantation promotes an unsustainable spare-parts approach to healthcare. It deemphasizes the importance of preventive health programs and lifestyle changes such as dieting, exercise and smoking cessation which could reduce the need for transplants of all kinds.

Breeding Animals For Food is Unhealthy and Does Not Justify Xenotransplantation

The HHS maintains that using animals such as pigs as xenograft donors is justified because pigs are "currently commercially bred and raised as a source of food" (p.49920). However, the same industry which disregards farm animals and views them as exploitable commodities, will likely disregard animals raised for xenotransplantation. Our traditional agricultural sector currently engages in unsanitary practices which place the health of both animals and humans at risk.

Animal feeding practices have come under increasing scrutiny for their ability to cause disease in animals and humans.¹⁵³ The American Association of Feed Control Officials lists dried poultry manure, dried broiler litter, dried cattle waste, and pig waste as approved feed ingredients. Manure, animal remains and garbage are known to contain pathogens such as *E. Coli*, *salmonella*, *Listeria monocytogenes*, *Campylobacter jejuni*, *Yersinia enterocolitica*, *Clostridium botulinum*, tapeworms, as well as drug residues, toxic chemicals, and a variety of viruses.¹⁵⁴ Human Creutzfeldt-Jakob Disease has been linked to the practice of feeding cows the ground up remains of other animals.¹⁵⁵

While the HHS specifies that "recycled or rendered animal materials" should be excluded from the feed of "source animals" (paragraph 3.2.1.3), such practices may be impossible to monitor and control since breeding facilities will largely be self-monitoring operations. This is not reassuring because feed laws are routinely violated in traditional animal husbandry operations as farmers seek to cut costs, in spite of federal oversight.¹⁵⁶ Because breeding and/or cloning animals for the xenotransplantation market would be undertaken as a for-profit venture, the industry would be subject to the

same economic pressures that currently exist in the traditional agricultural sector. It will be difficult, therefore, to maintain sanitary conditions in the source animal breeding facilities.

Regulations, which will likely be heavily influenced by the xenotransplant industry to begin with, may not be complied with rigorously, leading to breaches of protocol, with potentially devastating consequences for human health, animal health, and the environment.

Eating and Breeding Animals is What Makes People Sick; Prevention is Essential

The message that transplantation sends to doctors and scientists is that disease prevention needn't be emphasized; the message conveyed to the public is that it is not necessary to take responsibility for our own health by eating properly and exercising, or avoiding cigarettes and alcohol, because we can expect medical "miracles" to save us. Indeed, the number of patients with preventable diseases for which transplants are prescribed as a treatment, is growing.¹⁵⁷ The number of transplants performed continues to grow, with demand outstripping supply, all of which places a tremendous strain on our health care system and economy.

Ironically, it is precisely because people eat too many pigs (and other factory-farmed animals), and have unhealthy lifestyles, that pig organ transplants are being considered. Alcohol-related cirrhosis and alcoholic hepatitis are the most common forms of fatal liver disease in the US, which could be prevented through avoidance of alcohol.¹⁵⁸ Similarly, about 5,000 intravenous drug users develop a chronic and potentially fatal form of hepatitis C every year¹⁵⁹ which could be prevented through avoidance of drugs, or needle sharing. A study published in *Preventive Medicine*

(November 1995) revealed that meat-eating is responsible for \$61.4 billion in annual health care costs.¹⁶⁰

Diabetes is the most common condition found in patients who need kidney transplants,¹⁶¹ and it is largely controllable through diet and lifestyle changes.

Scholars, scientists and physicians¹⁶² have criticized the current animal-centered food production system as environmentally destructive, inhumane, unhealthy, and unsustainable. Pig farmers suffer high rates of respiratory ailments, pneumonia, lung scarring, animal bites, and chemical poisoning.¹⁶³ New deadly, antibiotic-resistant strains of *salmonella* (DT104) - linked to farm animals, pork sausage, meat paste and raw chicken,¹⁶⁴ and E-Coli (O157:H7) - long-associated with tainted beef,¹⁶⁵ are invading the US.

We Should Be Investing In Alternatives to Xenotransplantation

It is unclear who would pay to implement the HHS's extremely costly guidelines. Before allocating US funds to such an undesirable technology as xenotransplantation, federal public health agencies have a duty to explore proven, less costly and less risky alternatives. These include investing in preventive health and health maintenance programs. Lifestyle changes have proven capable of reversing heart disease.¹⁶⁶ An article in the *Journal of the American Dietetic Association* suggested that \$13 billion in medical costs could be saved and 100,000 first-time heart attacks averted by the year 2005 if Americans simply reduced their average saturated fat intake by one to three percentage points.¹⁶⁷ Many examples of preventive medicine could drastically reduce the demand for human organs (and surgical procedures of all kinds), thereby eliminating the prospect of cross-species transplants. The American Society of Primatologists,

and several animal advocacy organizations, strongly encourage their members to become organ donors, either through the mechanism of driver's license renewal or through signing an organ donor card (available through the United Network for Organ Sharing).¹⁶⁸ Launching government-funded education campaigns aimed at increasing the pool of human organs should be considered. Neither the government nor the medical community have aggressively encouraged human organ donation.¹⁶⁹ Currently, only 20% of those individuals who die "healthy" have arranged to donate their organs, even though a 1993 Gallup Poll showed that 85% of the public supports organ donation.¹⁷⁰

Presumed consent legislation has been enacted in several countries. The law presumes that everyone is an organ donor unless they specify otherwise. When Belgium enacted its presumed consent law in 1986, organ donation increased by 183% in a two-year period.¹⁷¹ Organ availability quadrupled in Austria when its law was enacted.¹⁷² A 1996 Swedish law requires all citizens to make a decision regarding the use of their organs after death, and has increased the donor pool by 600,000. A similar Danish law increased the donor population by 150,000.¹⁷³ If presumed consent legislation were enacted in the US, researchers contend that 75% of the adult US population (210,000,000) would become committed potential organ donors.¹⁷⁴

But Lloyd Cohen, Professor of law at George Mason University in Virginia, claims that, the US organ shortage (of some 50,000 organs per year) could easily be alleviated by creating financial incentives or rewards for donors. Potential donors would sign a contractual agreement, similar to a life insurance policy, designating beneficiaries of their choice (relatives or friends).

Should a donor die and his/her organs be harvested to save another person's life, the donor's beneficiaries would collect the proceeds from the "sale" of those organs.¹⁷⁵

We could also be investing in the development of synthetic organs and other surgical techniques to repair malformed or poorly functioning organs. About 75% of patients who undergo a procedure called ventricular remodeling - in which a section of heart muscle is removed and reshaped - can be taken off the transplant waiting list.¹⁷⁶

Ultimately, the MRMC believes that transplantation is a dangerous and expensive approach to healthcare which should not become a normative treatment modality. Physicians and health care agencies need to focus their energies and resources on education and prevention programs to avoid the need for transplants of all kinds.

V. Economic Concerns:

Because of its exorbitant price tag, xenotransplantation threatens to drive up health care costs for a majority of Americans, placing an unacceptable financial burden on the federal government, both in terms of financing the procedures and the postoperative care, and in dealing with the consequences of a potential viral epidemic akin to HIV or worse. Less costly alternatives to xenotransplantation exist and should be explored.

Human-to-Human Transplants Are Expensive

Approximately 76,000 patients were referred for organ transplants in 1996, with the majority of those (45,545) being corneal transplants.¹⁷⁷ But human-to-human transplants are in and of themselves expensive, with average hospital and first-year postoperative care averaging \$200,000 per patient in 1996 dollars¹⁷⁸ - more than double what it cost to treat a

person with HIV from diagnosis to death in 1994 (circa \$60,000).¹⁷⁹ Costs are rising and five-year survival rates have decreased slightly.¹⁸⁰ Estimated postoperative costs (for liver patients), including anti-rejection drugs and other medications, are approximately \$11,000 in the first year, and up to \$18,500 annually in the years to follow. Immunosuppressive medications are required for the rest of the recipient's life; he/she must also be continually monitored for infection, rejection, and graft arteriopathy.¹⁸¹ There are fees for lab tests, child care, physical and occupational therapy and rehabilitation, among other things.¹⁸² Some patients must have several transplants during their lifetimes to replace failing organs.¹⁸³

Despite the use of immunosuppressive drugs, roughly 50% of transplanted human organs are rejected and fail within five years.¹⁸⁴ (Rejection problems would clearly be worse for xenotransplants). Besides the problems of rejection, and toxicity from immunosuppressive drugs (doses of which would likely be increased in xenotransplants), the threat of infectious disease is also an issue in allotransplantation. The HHS admits (p.49921) that "transmission of infections (HIV/AIDS, Creutzfeldt-Jakob Disease, rabies, hepatitis B, hepatitis C) via transplanted human allografts has been well documented."¹⁸⁵ Given the above, one must question whether the costs associated with allotransplantation are presently justifiable, particularly when a majority of these procedures could be avoided.

Procuring human organs for transplantation is not without its ethical controversies either. In the 1980s it was feared that poor people in developing countries were being killed so their organs could be harvested and exported to the developed world.¹⁸⁶ Between 1990 and 1995, more than 2000 kidneys, were sold annually to

wealthy Middle Eastern recipients.¹⁸⁷ Questions have resurfaced about whether terminally ill patients' deaths are being hastened at some US hospitals to obtain their organs for transplant.¹⁸⁸ In addition, the concept of brain death has been questioned, which has stirred debates about "when to call someone dead."¹⁸⁹ Some have said that current criteria offer no guarantee that a patient is indisputably dead.¹⁹⁰ Surgeons and others in the transplant community fear that the publicity surrounding this issue will frighten people and discourage them from becoming organ donors.¹⁹¹

Xenotransplants Will Be Even More Expensive

Xenotransplantation is riskier and promises to be even more expensive than allotransplantation (\$250,000 per operation in 1995,¹⁹² not including the costs of breeding, housing, feeding, medicating, testing, transporting, rendering, and disposing of the waste and remains of herds of transgenic animals).¹⁹³ Institute of Medicine figures from 1996 reveal that xenotransplant costs for all patients who need organs could reach \$20.3 billion.¹⁹⁴ These costs are beyond the means of the average health care consumer and an already overburdened health care system. Xenotransplantation is excluded by Medicare and Medicaid and denied by health maintenance and preferred-provider organizations. If ever successful, xenotransplantation would, at best, benefit a small minority of patients (100,000) while dramatically driving up health care costs for all Americans. This is fiscally irresponsible.

Ironically, the AIDS epidemic appears to have reduced the number of potential (human) organ donors due to the threat of infection.¹⁹⁵ Unleashing a xenogeneic infection in the human population via xenotransplantation could have a similar effect: as more and more people became infected with a new zoonotic virus, the number of

“biotechnology and pharmaceutical companies are eager to cash in on the promise of a booming xenotransplantation market”

available human organs for transplantation would shrink accordingly. Thus, in an attempt to solve one problem, xenotransplantation could create another, driving costs for conventional (human) organ transplants even higher.

Xenotransplants Are Not a Given Yet

The Institute of Medicine's June 1996 report, *Xenotransplantation: Science, Ethics, and Public Policy*, concluded that “the potential benefits of

xenotransplants are great enough to justify the risk.” The report was funded by parties who are hardly neutral in this debate, including the FDA, the National Institutes of Health through the National Cancer Institute, and the US Department of Defense (all champions of animal-based

research), Charles River Laboratories (breeders of animals used in experimentation), and W. R. Grace and Company (whose subsidiary, American Breeders Service (ABS) filed a patent (WO 95/17500) in 1993 to cover clones and chimeras from pigs, horses, cows, antelopes, goats, and sheep bred with desirable traits for agricultural purposes). Researchers and biotechnology companies are eager to begin mass producing herds of transgenic animals, to provide a potentially limitless supply of organs for transplantation into humans.

The HHS seems to hint that, despite the inherent public health risks, “the commercialization of xenograft production . . . throughout the US and the world” (p.49920) is imminent and inevitable - an inappropriate stance for an allegedly neutral public health agency.

The HHS fails to speak of the lobbying power of special interests in the decision-making process. A recent issue of *Fortune* magazine revealed that biotechnology and pharmaceutical companies are eager to cash in on the promise of a booming xenotransplantation market - worth \$6 billion annually (and 450,000 pig organ transplants) by 2010.¹⁹⁶ Pharmaceutical giants like Sandoz Pharma AG (US and Switzerland), Bristol-Meyers Squibb, Hoechst, Fujisawa, and biotechnology companies like Alexion Pharmaceuticals Inc. (New Haven, CT), Nextran Corp. (Princeton, NJ), Biotransplant, Inc. (Charlestown, MA), and Imutran (recently acquired by Sandoz), all have a stake in this market. Public health authorities should not be placing the interests of these private corporations and their lobbyists over the interests of the American public.

The Environmental Problems Posed By Xenotransplantation

The adverse environmental and health impacts of animal-based agriculture have been well-documented.¹⁹⁷ Nonpoint source pollution, such as agricultural waste, is now the principle threat to surface and ground water quality in the US.¹⁹⁸

North Carolina State University estimates that hundreds of hog manure lagoons, needed as part of hog productions in the state are leaking contaminants such as nitrate - a chemical linked to “blue baby syndrome” - into the groundwater.¹⁹⁹ No mechanical method of retrieval exists to clean contaminants from groundwater. In the summer of 1995, a hog manure lagoon broke open and released 25 million gallons of waste from 10,000 hogs into nearby waters and on to neighboring soybean and tobacco fields.²⁰⁰

A deadly microscopic phytoplankton named *Pfiesteria piscida* (latin for fish-

killer) thrives in waters polluted by hog manure. The organism can change into 22 different forms - from an amoeba to a two-tailed killer that drugs schools of fish and sucks off their skin. It has been blamed for killing half the fish stocks in North Carolina in the 1990s. After allegedly becoming airborne, *Pfiesteria* caused North Carolina University freshwater botanist Joann Burkholder and a colleague to become ill with headaches, asthma, stomach cramps, nausea, vomiting, memory loss, and muscle weakness. Fearing a loss of tourism and retribution from the hog farming industry, state officials have refused to accept the existence of a problem or to issue health warnings, accusing Burkholder and others of being drunk or fabricating their ailments.²⁰¹

Many experts have addressed the problem of farm animal carcass and waste disposal. Kenneth Steele, Professor in the Department of Geology at the University of Arkansas, Fayetteville, writes that “the use or disposal of animal wastes directly impacts the quality of the land and water.”²⁰² Charles D. Fulhage, of the Department of Agricultural Engineering at the University of Missouri, Columbia writes that “Improper disposal of dead animals can result in surface water or groundwater contamination.”²⁰³ John M. Sweeten, extension agricultural engineer specializing in waste management at Texas A & M University reported that livestock manure (from holding ponds, treatment and storage lagoons, and manure stockpiles), contains pathogenic organisms, nitrates, ammonia [and bacteria and viruses] that can contaminate groundwater.²⁰⁴ Pathogenic water-borne organisms in manure include *Salmonella*, *listeria*, *vibrio*, *brucella*, *cryptosporidium*, *coxiella*, *chlamydia*, and *mycoplasma*.²⁰⁵ *Cryptosporidium* in calf waste was blamed for a 1993 outbreak in Milwaukee that left 400,000 people sick and more than 100 dead.²⁰⁶

Pesticides and insecticides (commonly used in agriculture), and their by-products may also contribute to soil and groundwater contamination.²⁰⁷

How would facilities breeding pigs for xenotransplants deal with the waste generated by their facilities, particularly in light of recent knowledge about microorganisms like *Pfiesteria*? Would they deny or try to cover up public health dangers? And how would they dispose of transgenic pigs' bodies once their organs were harvested?

Conventional agricultural operations and rendering plants continuously wrestle with the problem of how to dispose of millions of tons of perishable animal tissue each year.²⁰⁸ A February 1992 article by Kenneth B. Kephart, Extension Swine Specialist for the Department of Dairy and Animal Science at Penn State University, exposed Pennsylvanian farmers' concerns about how to dispose of 100,000 dead hogs annually: by-products of their industry. Incineration,²⁰⁹ burial, and composting²¹⁰ were all described as expensive, unhygienic, and environmentally problematic options. Burial is recognized as an undesirable option due to the potential for groundwater contamination by rotting and diseased flesh.²¹¹

HHS seems to favor the marriage of agriculture and medicine by way of a close collaboration between animal breeding facilities and hospitals/research centers. But in paragraph 3.2.1 of its guidelines, HHS makes no mention of how biomedical animal facilities are to dispose of the numerous remains of genetically modified animals and their offspring. Nor does it make any mention of the environmental impact such facilities would have on local communities - an extremely important omission in the context of the potential disease risks posed by the disposal of such remains.

The responsibility is left to the facility, which is not reassuring given the numerous institutional scandals described herein.

VI. Conclusion

Research has demonstrated that the risk of transmitting animal viruses to humans is real. This is a concern to scientists worldwide. In a letter to the journal *Emerging Infectious Diseases*, French virologist Claude Chastel wrote that, "while we face the terrific threat of AIDS . . . we are preparing a new infectious 'Chernobyl.'" Chastel is among dozens of virologists who have publicly advocated a moratorium on xenotransplantation.²¹²

The HHS proposed guidelines on xenotransplantation procedures acknowledge the dangers the technology could pose to xenograft recipients, laboratory and health care workers, and society at large. Despite this fact, federal health authorities have yielded to the positions held by biotechnology companies, anti-regulation forces, and transplant lobbies, excluding the public and xenotransplantation's critics from debates.²¹³ This has led to irresponsible policy-making and to the development of unnecessary, expensive, clinically unproven, and potentially dangerous new drugs and technologies.

Before supporting a treatment option like xenotransplantation, government and private granting agencies should be allocating funds to 1) prevention programs aimed at reducing the need for transplants of all kinds, 2) administrative programs to increase human organ donations, and 3) - reflecting society's growing respect and compassion for the nonhuman world²¹⁴ - technologies which lessen our dependence on animals.

Given our society's poor track record in managing modern global threats including the increasing lethality of military weapons, environmental pollution, rainforest destruction,

exponential population growth, and diseases like AIDS, we must honestly ask ourselves whether we have the wisdom and moral maturity needed to deal with the consequences of xenotransplantation and related genetic technology. Until that question is publicly debated and, if ever, answered, logic dictates a policy of restraint and humility.

In light of the epidemiological, public health, medical, scientific, economic, and environmental issues outlined in this critique, the MRMC advocates an indefinite freeze on all forms of experimentation and clinical application of xenotransplantation technology. Federal funds should not be used to fund any stage of xenotransplantation's development.

Alix Fano, M.A.

Murry J. Cohen, M.D.

Marjorie Cramer, M.D.

Ray Greek, M.D.

Stephen R. Kaufman, M.D.

References

- 1 Anthony Dorling, et al., 'Clinical Xenotransplantation of Solid Organs,' *The Lancet* 349 (March 22, 1997): 867-71.
- 2 David Stipp, 'Replaceable You,' *Fortune*, November 25, 1996, pp.131-138.
- 3 Lawrence K. Altman, 'Hope in AIDS Case is Put in Marrow From Baboon,' *The New York Times*, December 15, 1995, p.A1; Jeremy Laurance, 'Takeover Increases Chance of Pig Hearts in Humans,' *The Times*, London, 18 April 1996; Susan E. Paris, 'Animal Transplants Extend Medical Gains,' *The New York Times*, September 25, 1996, letters p.A20.
- 4 In a statement to the Food and Drug Administration, 44 physicians, veterinarians, scientists, and professors of medicine stated that "xenotransplantation poses a serious risk to the public health ..." Statement submitted by Jonathan S. Allan of the Southwest Foundation for Biomedical Research in San Antonio, Texas to Dr Timothy W. Beth, Consumer Safety Officer at the Food and Drug Administration, December 20, 1996.
- 5 Associated Press, 'Doctors Petition University to End Baboon Transplants,' *Newark Star-Ledger*, February 7, 1993; letter submitted to Stephen Dorrell, British Secretary of State for Health by Andre Menache, President, Doctors and Lawyers for Responsible Medicine, London; comments submitted to the Food and Drug Administration by Neal D. Barnard, President, Physicians Committee for Responsible Medicine, Washington, DC, on behalf of the organization's 4,000 physician and 70,000 lay members, December 19, 1996.
- 6 Some critics claim that they may be better described as pig endogenous retroviral sequences (PERS) since the PERV definition implies that actual "viruses" exist in all pig cells. Letters to the editor, *Nature Medicine* 3, no. 5 (May 1997): 474.
- 7 Laurie Garrett, 'Pig Virus Called Human Threat,' *New York Newsday*, November 14, 1996, p.A37.
- 8 Clive Patience, et al., 'Infection Of Human Cells By An Endogenous Retrovirus of Pigs,' *Nature Medicine* 3, no. 3 (March 1997): 282-6; Jacqui Wise, 'Pig Virus Transfer Threatens Xenotransplantation,' *British Medical Journal* (1 March 1997): 623.
- 9 Peter Wheale, Ruth McNally, eds., *The Bio Revolution: Cornucopia or Pandora's Box* (London: Pluto Press, 1990), 31-54.
- 10 Rodney Barker, *And the Waters Turned to Blood* (New York: Simon & Schuster, 1997).
- 11 Marian Burros, 'US Is Asked to Take New Steps to Prevent Mad Cow Disease,' *The New York Times*, March 28, 1997, p.A17.
- 12 J. P. Stoye, J. M. Coffin, 'The Dangers of Xenotransplantation,' *Nature Medicine* 1 (1995): 1100; D. M. Smith, 'Endogenous Retroviruses in Xenografts,' *New England Journal of Medicine* 328 (1993): 142-3.
- 13 Anon, 'From the Belly of the Beast,' *The Economist*, October 21, 1995, p.83-84.
- 14 Frederick A. Murphy, 'The Public Health Risk of Animal Organ and Tissue Transplantation into Humans,' *Science* 273 (9 August 1996): 746-747.
- 15 Personal communication with Moneim Fadali, Diplomate American Board of Surgery and American Board of Thoracic Surgery, Los Angeles, California, May 6, 1996.
- 16 Lawrence K. Altman, 'Cross-Species Transplants Raise Concerns About Human Safety,' *The New York Times*, January 9, 1996, p.C11.
- 17 Jacqui Wise, 'New Authority to Monitor Xenotransplantation Experiments,' *British Medical Journal* 314 (25 January 1997): 247; Kelly Morris, 'No Early Rejection of Animal Organs in UK,' *The Lancet* 349 (25 January 1997): 257.
- 18 Jonathan S. Allan, 'Xenotransplantation at a Crossroads: Prevention Versus Progress,' *Nature Medicine* 2, no.1 (January 1996): 18.
- 19 Thomas E. Starzl, et al., 'Baboon-to-Human Liver Transplantation,' *Lancet* 341 (1993): 65-71; Jonathan S. Allan, (1996): 19.
- 20 James W. Ebert, Louisa E. Chapman, Amy P. Patterson, 'Xenotransplantation and Public Health,' *Current Issues in Public Health* 2 (1996): 215-19.
- 21 Violations of public health regulations, let alone voluntary guidelines, are common in the US and elsewhere. Hospitals have violated laws regulating blood supplies; and states regularly ignore environmental laws. John H. Cushman, Jr., 'States Neglecting Pollution Rules, White House Says,' *The New York Times*, December 15, 1996, p.A1.
- 22 Jonathan S. Allan, (1996): 18.
- 23 Jonathan S. Allan, 'Public Health Concerns Take Center Stage in Nuffield Council on Bioethics,' *Science and Engineering Ethics* 2, no. 4 (1996): 486-90.

- 24 Jonathan Allan, 'Silk Purse Or Sow's Ear,' *Nature Medicine* 3, no. 3 (1997): 275-6.
- 25 In April 1996, the Ebola virus was discovered in the US, at the South Texas Primate Center near Alice in two or three monkeys imported from the Philippines for research. Luckily in this case, no human fatalities were reported; fatality rates among humans exposed to Ebola approach 90%. Fifty animals had to be killed and their carcasses incinerated. Laboratory workers were placed under observation, rather than in quarantine. The strain of the Ebola virus in question was identified as "Ebola Reston," named for the 1989 outbreak in Virginia. Murry J. Cohen, 'Ebola Alice,' *Texas Republic*, Summer 1996, pp.27-30.
- 26 Pearce Wright, 'Smallpox Vaccine "Triggered AIDS Virus,"' *The London Times*, 11 May 1987, p.1.
- 27 In the 1950s and 1960s, the (Salk) polio vaccine (made from the renal cells of rhesus and cynomolgus monkeys) was contaminated with the SV-40 virus, now suspected of causing human cancer. Pat Wechsler, 'A Shot in the Dark,' *New York Magazine*, November 11, 1996, pp.38-43, 85; Anon, 'Monkey Virus in Polio Vaccine,' *JAMA* 277 (19 March 1997): 873.
- 28 S. S. Morse, A. Schluederberg, 'Emerging Viruses: The Evolution of Viruses and Viral Diseases,' *Journal of Infectious Diseases* 162 (1990): 1-7; World Health Organization, *World Health Report* 1996 (Geneva: WHO, 1996); Laurie Garrett, *The Coming Plague* (New York: Penguin Books, 1995).
- 29 Anon, *The Economist*, (October 21, 1995), 84.
- 30 Jonathan S. Allan, 'Xenotransplantation at a Crossroads: Prevention Versus Progress,' *Nature Medicine* 2, no.1 (January 1996): 18-21; Jonathan S. Allan, 'Xenotransplantation and Possible Emerging Infectious Diseases,' *Molecular Diagnosis* 1, no. 3 (1996): 209-17.
- 31 Clive Patience, et al., (March 1997): 282-6.
- 32 Louisa E. Chapman, et al., (November 30, 1995): 1500.
- 33 Paul Recer for the Associated Press, 'Deadly 1918 Flu Outbreak Solved,' March 21, 1997; S. Sternberg, 'A Doughboy's Lungs Yield 1918 Flu Virus,' *Science News* 151 (March 22, 1997): 172.
- 34 Alison Boulton, 'Doctors Voice Virus Fears Over Xenotransplants,' *British Medical Journal* 312, (11 May 1996): 1186.
- 35 Associated Press, "'Pig Epidemic" Strikes in Remote Indonesia,' February 28, 1996.
- 36 Frederick A. Murphy (9 August 1996): 746-747.
- 37 Susan S. Ellenberg, Robert T. Chen, 'Vaccine Safety,' *Public Health Reports* 112 (January/February 1997): 11-20.
- 38 Lawrence K. Altman, '153 Hepatitis Cases Are Traced to Frozen Imported Strawberries,' *The New York Times*, April 3, 1997, p.A1; Associated Press, 'Possibly Tainted Berries Sent to 17 States,' *The New York Times*, April 2, 1997; Tom Curley, 'Hepatitis Probe,' *USA Today*, April 7, 1997, p.3A.
- 39 David Johnston, 'Report Criticizes Scientific Testing at FBI Crime Lab,' *The New York Times*, April 16, 1997, p.A1.
- 40 Jane Ellen Stevens, 'New Project Investigates Mystery Deaths and Illnesses,' *The New York Times*, March 25, 1997, p.C1.
- 41 Ibid., p.C1.
- 42 Robert E. Michler, 'Xenotransplantation: Risks, Clinical Potential, and Future Prospects,' Source: Internet address, <http://www.medscape.com/Clinical/other/...02.n01/e2110.michler>, November 1, 1996.
- 43 Jonathan S. Allan (1996): 20.
- 44 Jane Ellen Stevens, (March 25, 1997), p.C1.
- 45 Panos Dossier, *AIDS and the Third World* (Philadelphia: New Society Publishers, 1989), 122.
- 46 See for example P. D. Cleary, et al., *JAMA* 258 (2 October 1987): 1757-1762.
- 47 Jonathan S. Allan, *Molecular Diagnosis* (1996): 213.
- 48 Susan Gilbert, 'Doctors Often Misread Results of Genetic Tests, Study Finds,' *The New York Times*, March 26, 1997, p.C8.
- 49 Panos Dossier, 1989, 122.
- 50 Dan Barry, 'US Energy Chief Removes Manager for Brookhaven,' *The New York Times*, May 2, 1997, p.A1.
- 51 Dan Barry, 'At 50, Brookhaven Lab is Beset by Problems,' *The New York Times*, March 22, 1997, p.1; Associated Press, 'Brookhaven Lab Reports New Radioactive Leaks,' *The New York Times*, March 28, 1997, p.B6.
- 52 Charles Fleming, 'France Levies Tax to Help Victims of AIDS Scandal,' *The Wall Street Journal*, November 29, 1991; Richard Tomlinson, 'Chinese Clamp Down on Blood Products,' *British Medical Journal* 314, (11 January 1997): 93.

- 53 The Associated Press, 'Company Kept Blood-Clotting Drug on Market Despite Warnings,' October 5, 1995. Armour forbade Alfred Prince, the scientist who warned the company about its failed heat-treating process, from making his findings public.
- 54 The case was settled for \$670 million. Reuters, '4 Drug Companies Ordered to Pay Hemophiliacs,' *The New York Times*, May 8, 1997, p.D12.
- 55 Source: <http://www.web-depot.com/hemophilia/archives/nyt-1996-04-19>
- 56 The Blood Center closed its screening lab in Manhattan under pressure from the Food and Drug Administration. Lawrence K. Altman, 'Blood Center to Shut Down Screening Lab,' *The New York Times*, May 15, 1997, p.B3; Jan Hoffman, 'Investigations of Blood Center Lead to Former Worker's Arrest,' *The New York Times*, April 1, 1997, p.B3; David Stout, 'Blood Center to Revamp Its Testing and Training,' *The New York Times*, December 17, 1996, p.B3.
- 57 Philip Elmer-Dewitt, 'Turning the Tide,' *Time*, December 30, 1996/January 6, 1997, p.54.
- 58 Sales of antiviral drugs for AIDS reached \$1.3 billion in 1995. Andrew Purvis, 'The Global Epidemic,' *Time*, December 30, 1996/January 6, 1997, p.78.
- 59 Christine Gorman, 'The Disease Detective,' *Time*, December 30, 1996/January 6, 1997, p.64.
- 60 Sheryl Gay Stolberg, "'Unchecked' Experiments on People Raise Concern," *The New York Times*, May 14, 1997, p.A1.
- 61 New evidence gives validity to these concerns. Denise Grady, 'Study Finds Secondhand Smoke Doubles Risk of Heart Disease,' *The New York Times*, May 20, 1997, p.A1.
- 62 Matthew L. Wald, 'Rule Adopted to Prohibit Secret Tests on Humans,' *The New York Times*, March 29, 1997, p.7.
- 63 Jonathan S. Allan, 'Fear of Viruses,' *The New York Times*, January 20, 1996, Op-Ed.
- 64 Charles Fleming, (November 29, 1991).
- 65 Philip J. Hilts, 'Researchers Say Chemicals May Have Led to War Illness,' *The New York Times*, April 17, 1996, p.A17.
- 66 Matthew L. Wald, (March 29, 1997), p.7.
- 67 Lynda Richardson, 'Lives Ruined at Tuskegee,' *The New York Times*, April 21, 1997, p.B4. In 1932 the US Public Health Service allowed 399 poor black men with syphilis to go untreated for 40 years so the disease could be studied. The government has paid more than \$9 million in an out-of-court settlement to victims, their families and heirs.
- 68 Associated Press, 'Vietnam Veterans Expecting Agent Orange Benefits Soon,' *The New York Times*, January 3, 1989.
- 69 Harry Nelson, 'Claims Swamp US Agency That Pays for Vaccine Injuries,' *Los Angeles Times*, June 20, 1991, p.A5; Frank Jackman, 'Vaccine Suits OKd,' *Daily News*, June 14, 1988; A. R. Hinman, 'DTP Vaccine Litigation,' *Am J Dis Child* 140 (1986): 528-30.
- 70 Pat Wechsler, (November 11, 1996), 85.
- 71 Richard Nicholson, 'If Pigs Could Fly,' *Nursing Times* 93, no. 6 (February 5-11, 1997): 20.
- 72 Frederick A. Murphy (9 August 1996): 747.
- 73 D. G. Hoel, et al., 'Implications of Nonlinear Kinetics in Risk Estimation in Carcinogenesis,' *Science* 219 (1983): 1032-1036.
- 74 For an elaboration of this argument and references, see Edith Efron, *The Apocalypstics: Cancer and the Big Lie* (New York: Simon & Schuster, 1984).
- 75 Neal Barnard, S. Hou, 'Inherent Stress - the Tough Life in Lab Routine,' *Lab Animal* 17 (1988): 21-7; Gio Batta Gori, 'The Regulation of Carcinogenic Hazards,' *Science* 208 (18 April 1980): 256-61; Paul Cotton, 'Animals Benefit From "Replace, Reduce, Refine" Effort,' *JAMA* 270 (22 -29 December 1993): 2906.
- 76 The Association of Veterinarians for Animal Rights, an advocacy group in Davis, California, has stated that "Failure to articulate the morally relevant differences between [nonhuman] animals and the humans who will [allegedly] benefit from their deaths is ethically suspect . . ." Moreover, the group points out that transgenic animals are currently offered no protections under the US Animal Welfare Act or other government regulations. Gary Block, DVM, Association of Veterinarians for Animal Rights, comments to the HHS on "Guidelines on Infectious Disease Issues in Xenotransplantation," December 20, 1996.
- 77 John Robbins, *Diet For a New America* (New Hampshire: Stillpoint, 1987), 73-81.
- 78 Institute of Medicine, 'Xenotransplantation: Science, Ethics and Public Policy,' (Washington, DC: National Academy Press, June 1996).

- 79 British Union for the Abolition of Vivisection (BUAV), 'Insight Into Xenotransplantation, (London: BUAV, undated).
- 80 The Advisory Group on the Ethics of Xenotransplantation, *Animal Tissue Into Humans* (London: Department of Health, 1997).
- 81 Frederick A. Murphy (9 August 1996): 747.
- 82 Anon, 'Those Corrupting Prions,' *The Economist*, April 27, 1996, p.90.
- 83 Clive Patience, et al., (March 1997): 285.
- 84 Charles River Laboratories, 'A Laboratory Animal Health Monitoring Program: Rationale and Development,' (Winter 1990); Source: Internet address, <http://www.criver.com/techdocs/hmradev.h> as of July 1996.
- 85 Murry J. Cohen, 'Risks of Importing Monkeys,' *The Washington Post*, May 6, 1996, Letter to the Editor; Barbara Nasto, 'Philippine Monkey Facility Closed,' *Nature Medicine* 3, no. 3 (March 1997): 263.
- 86 Paul Brown, et al., "'Friendly Fire' In Medicine: Hormones, Homografts and Creutzfeldt-Jakob Disease," *The Lancet* 340 (4 July 1992): 24-7.
- 87 M. M. Robinson writes that "Infection with transmissible encephalopathies is difficult to predict or control," and the pathogens are difficult to detect. M. M. Robinson, 'Transmissible Encephalopathies and Biopharmaceutical Production,' *Developments in Biological Standardization* (Basel) 88 (1996): 237-41.
- 88 Anon, "'Mucca Pazza,' Italia Terza in Europa Per Numero di Casi,' *Il Mattino*, 11 October, 1996, p.9; Massimo Novelli, 'Mucca Pazza, S'Indaga Su Una Morte Sospetta,' *La Repubblica*, 12 October, 1996, p.17; Luigi Grimaldi, 'Mucche Pазze, Allarme a Verona,' *Il Messaggero*, 7 April, 1996, p.6. "Mad" cows have also been identified in Canada, Denmark, France, Germany, Ireland, Portugal, and Switzerland. Source: <http://www.cspinet.org/>
- 89 Reuters, 'Dutch Report Mad-Cow Disease,' *The New York Times*, March 22, 1997, p.2.
- 90 Warren Hoge, 'Major, Feeling Political Heat, Plans to Step Up Slaughter of Cows,' *The New York Times*, December 17, 1996, p.A15.
- 91 Anon, 'Europeans at Risk From Mad Cow Disease,' Source: Internet address <http://envirolink.org/arrs/news/mad-cow1.html>, August 10, 1995, as of December 12, 1996.
- 92 Anon, 'Tories Are Accused On "Mad Cow" Study,' *The New York Times*, March 7, 1997, p.A8.
- 93 Anon, 'The Other BSE Scandal,' *The Economist*, February 22, 1997, pp.61-2.
- 94 Ildstad's work (which was largely carried out in mice) has been criticized by physicians, immunologists, infectious disease experts, and other xenotransplant researchers. Lawrence K. Altman, 'When Doctors and Patients Decide to Test the Far Limits of Treatment,' *The New York Times*, December 19, 1995, p.C3. Some have questioned her discovery of a new type of bone marrow (facilitator) cell which, when mixed with typical stem cells from the marrow of a donor, averts the problems associated with hyperacute rejection. Apparently, no scientists besides Ildstad have been able to identify these special facilitator cells. Gina Kolata, 'Transplant: Urgent Step or Step Off the Edge,' *The New York Times*, January 9, 1996. In reality, writes John McArdle, Ph.D., "baboon cells may not be resistant to HIV, foreign marrow cells may not function in an environment regulated by human hormones and physiology, and new immune cells may not be able to develop in AIDS patients with typically damaged thymus glands." John McArdle, 'Xenotransplantation and Primates,' *The AV Magazine*, Primates Issue, Fall 1996, pp.14-17.
- 95 Steven Benowitz, 'Xenotransplantation Pioneer Planning to Expand Her Focus,' *The Scientist*, October 28, 1996, p.9. Ildstad said, "it was a wise decision (for the FDA) to recommend procedures to diminish transmission of infection to the recipient rather than regulate. There's a huge difference in the FDA between something that's "regulated" and something that has "guidelines for a procedure" . . . I feel very reassured that the FDA seems to feel . . . that the potential benefits . . . by far outweighed the risks."
- 96 Jonathan S. Allan, 'Xenotransplantation at a Crossroads: Prevention Versus Progress,' *Nature Medicine* 2, no.1 (January 1996): 19.
- 97 Sheryl Gay Stolberg, (May 14, 1997), p.A16.
- 98 Tony Stark, *Knife to the Heart: The Story of Transplant Surgery* (UK: Macmillan, 1996), p.233.
- 99 Ibid., 11-13, 167.
- 100 See tables and references in S. Taniguchi, David K. C. Cooper, 'Clinical Xenotransplantation: Past, Present and Future,' *Annals of the Royal College of Surgery (England)* 79 (1997): 13-19.
- 101 Tony Stark, (1996), pp.19-20.
- 102 Ibid., p.20.
- 103 Ibid., p.21.

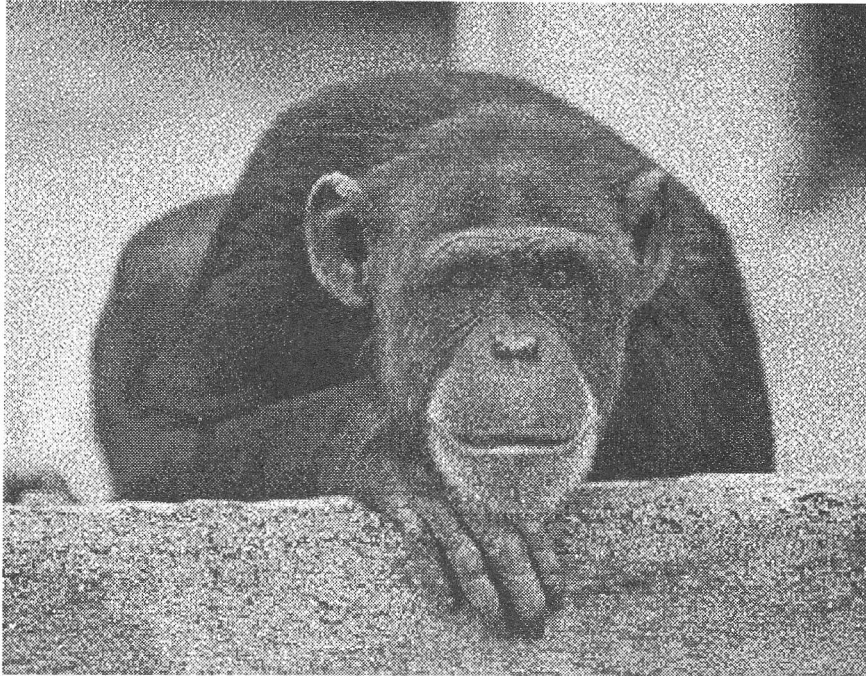
- 104 Ibid., p.158.
- 105 Ibid., pp.156-58, 159.
- 106 Ibid., p.231.
- 107 Ibid.
- 108 Ibid., pp.158-162.
- 109 D. N. Ross, *Experience With Human Heart Transplantation*, H. Shapiro, ed., (South Africa: Butterworths, 1969), 227-8; J. Czaplicki, et al., 'The Lack of Hyperacute Xenogeneic Heart Transplant Rejection in a Human,' *J. Heart Transplant* 11 (1992): 393-396; Tony Stark, (1996), p.233.
- 110 Tony Stark, (1996), p.231.
- 111 Anon, 'Grandstand Medicine,' *Nature* 312 (8 November 1984): 88.
- 112 Thomas E. Starzl, 'Baboon-to-Human Liver Transplantation,' *Lancet* 341 (9 January 1993): 65-71; Richard L. Worsnop, 'Organ Transplants,' *CQ Researcher* 5, no. 30 (August 11, 1995): 719.
- 113 Jonathan S. Allan, *Nature Medicine* 2, no.1 (January 1996): 18.
- 114 Richard L. Worsnop, (August 11, 1995): 719-20.
- 115 J. Czaplicki, et al., 'The Lack of Hyperacute Xenogeneic Heart Transplant Rejection in a Human,' *J. Heart Lung Transplant* 11 (1992): 393; D. R. Salomon, 'Invited Comment,' *J. Heart Transplant* 11 (1992): 396-7.
- 116 Richard L. Worsnop, (August 11, 1995): 719; BUAV, undated.
- 117 K. S. Jayaraman, 'Pig Heart Transplant Surgeon Held In Jail,' *Nature* 385, (30 January 1996): 398
- 118 Tony Stark, (1996), pp.45-6.
- 119 Ibid., p.70.
- 120 Ibid., p.158.
- 121 Ibid., p.58.
- 122 Ibid., p.163.
- 123 Ibid., pp.180-9.
- 124 British Union for the Abolition of Vivisection (BUAV), 'Insight Into Xenotransplantation,' undated.
- 125 Ibid.
- 126 Ibid.
- 127 Tony Stark, (1996), pp.176-7.
- 128 BUAV, undated.
- 129 See Tony Stark, *Knife to the Heart* (London: MacMillan, 1996).
- 130 Tony Stark, (1996), 177.
- 131 Lawrence M. Fisher, 'Down on the Farm, a Donor,' *The New York Times*, January 5, 1996, p.D1.
- 132 F. H. Bach, et al., 'Delayed Xenograft Rejection,' *Immunology Today* 17, no. 8 (August 1996): 379-84; Augustin P. Dalmaso, et al., 'Mechanism of Complement Activation in the Hyperacute Rejection of Porcine Organs Transplanted Into Primate Recipients,' *American Journal of Pathology* 140, no. 5 (May 1992): 1157-66; C. Chaussy, et al., 'Experimental Xenogeneic Kidney Transplantation In Closely Related Species. Transplantation of Cat Kidneys to Untreated and Sensitized Dogs,' *Res. Exp. Med. (Berlin)* 159, no. 4 (1973): 266-75.
- 133 Scott K. Pruitt, et al., 'Effect of Continuous Complement Inhibition Using ... On Survival of Pig-to-Primate Cardiac Xenografts,' *Transplantation* 63, no. 6 (March 27, 1997): 900-14; L. A. Valdivia, et al., 'Donor Transfusion in the Nude Rat ...,' *Transplant Proc* 29, no. 1/2 (February/March 1997): 928.
- 134 E. A. Davis, et al., 'Overcoming Rejection in Pig-to-Primate Cardiac Xenotransplantation,' *Transplant Proc* 29, no. 1/2 (February/March 1997): 938.
- 135 R. Heywood, 'Clinical Toxicity-Could it Have Been Predicted? Postmarket Experience,' in *Animal Toxicity Studies: Their Relevance For Man*, C. E. Lumley, S. R. Walker, eds., (London: Quay Publishing, 1989; A. P. Fletcher, *Journal of the Royal Society of Medicine* 71 (1978): 693-8; J. T. Litchfield Jr., *Clinical Pharmacology & Therapeutics* 3 (1962): 665-72; F. I. McMahon, *Medical World News* 6 (1965): 168.
- 136 Anon, 'The Clinical Impact of Adverse Event Reporting,' *MedWatch*, October 1996, published by the US FDA, Rockville, Maryland.
- 137 David J. Cohen, et al., 'Cyclosporine: A New Immunosuppressive Agent for Organ Transplantation,' *Annals of Internal Medicine* 101 (1984): 667-82.
- 138 In humans, Cyclosporine causes lymphoma, abnormal functioning of the kidneys or liver, growth of excess facial hair, mouth sores, and heightened sensitivity to heat and cold. Other anti-rejection drugs, including Prednisone, Imuran, and OKT-3 also have serious side-effects. Richard L. Worsnop, *CQ Researcher* (August 11, 1995): 714.

- 139 Anon, 'Cyclosporin For Ever?,' *The Lancet* (22 February 1986): 419-20; Richard L. Worsnop, (August 11, 1995): 714.
- 140 S. Taniguchi, David, K. C. Cooper, (1997): 18.
- 141 A. Hastillo, M. L. Hess, 'Heart Xenografting: A Route Not Yet to Trod,' *J. Heart Lung Transplant* 12 (1993): 3-4.
- 142 Robert E. Michler, (November 1, 1996).
- 143 Nuffield Council on Bioethics, *Animal-to-Human Transplants, The Ethics of Xenotransplantation* (UK, 1996).
- 144 World Health Organization, *The World Health Report 1996*, Executive Summary (Geneva: WHO, 1996), 1-6. Associated Press, 'Hantavirus Infection Claims a 4th Victim in Utah,' *The New York Times*, October 27, 1996, p.20.
- 145 See S. Taniguchi, David K. C. Cooper, (1997): 16; Anthony Dorling, et al., (March 22, 1997): 868.
- 146 S. Taniguchi, David K. C. Cooper, (1997): 16.
- 147 Donald Bruce, Director of the Church of Scotland, 'The Ethics of Xenografting,' Source: <http://webzone1.co.uk/www/srtproject/xennuf03.htm> as of March 3, 1997.
- 148 Richard Nicholson, 'If Pigs Could Fly,' *Nursing Times* 93, no. 6 (February 5-11, 1997): 20.
- 149 Tony Stark, *Knife to the Heart* (UK: Macmillan, 1996), 170.
- 150 Kelly Morris, (25 January 1997): 257; Richard L. Worsnop, (August 11, 1995): 714.
- 151 S. S. Kalter, R. L. Heberling, 'Xenotransplantation and Infectious Diseases,' *Institute of Laboratory Animal Resources Journal* 37 (1995): 32.
- 152 Louisa E. Chapman, et al., 'Xenotransplantation and Xenogeneic Infections,' *The New England Journal of Medicine* 333, no. 22 (November 30, 1995): 1500.
- 153 Sandra Blakeslee, 'Fear of Disease Prompts New Look at Rendering,' *The New York Times*, March 11, 1997, p.C1.
- 154 Eric R. Haapapuro, 'Piling it High and Deep,' *Good Medicine*, Autumn 1996, p.15, published by the Physicians Committee for Responsible Medicine, Washington, DC.
- 155 Anon, 'The BSE Scare: Mad Cows and Englishmen,' *The Economist*, March 30, 1996, pp.25-26.
- 156 The British Ministry of Agriculture Fisheries and Food maintains that most of the current cases of bovine spongiform encephalopathy (BSE) are a result of farmers breaking the law by continuing to use parts of cattle in livestock feed. 'Europeans at Risk From Mad Cow Disease,' August 10, 1995 Source: Internet address <http://envirolink.org/arrs/news/mad-cow1.html>, as of December 12, 1996. Lawrence K. Altman, 'US Officials Confident That Mad Cow Disease of Britain Has Not Occurred Here' *The New York Times*, March 27, 1996, p.5; Oliver Tickall, 'Now Industrial Waste Can Feed the Animals,' *Sunday Independent*, Ireland, May 5, 1996.
- 157 Robert E. Michler, (November 1, 1996).
- 158 Richard H. Hauboldt, *Cost Implications of Human Organ and Tissue Transplantation, An Update: 1996*, published by Milliman & Robertson, Inc., Minneapolis, Minnesota, p.17.
- 159 Associated Press, 'Experts Warn of a Tripling of Deaths From Hepatitis C by 2017,' *The New York Times*, March 27, 1997, p.A21.
- 160 Neal D. Barnard, et. al., 'The Medical Costs Attributable to Meat Consumption,' *Preventive Medicine* 24, (November 1995): 646-55.
- 161 Richard H. Hauboldt, (1996), 20.
- 162 Rod Usher, 'The Cadillac That Moos: Has the Cow Become a Luxury the Planet Can No Longer Afford?,' *Time*, April 1, 1996, p.25. See also Frances Moore Lappe (*Diet for a Small Planet*), Jim Mason (*Animal Factories*), Jeremy Rifkin (*Beyond Beef*), John Robbins (*Diet for a New America*), and the writings of C. R. Attwood, Neal Barnard, T. Colin (China Study) Campbell, W. Harris, Michael Klaper, John McDougall, Dean Ornish, and others.
- 163 Peter T. Kilborn, 'The Perils of Pig Farming Touch Man and Beast,' *The New York Times*, August 25, 1991, p.A1.
- 164 Associated Press, 'Resistant Salmonella Reaches United States,' *The New York Times*, April 11, 1997, p.A18.
- 165 Marian Burros, 'The Debate Over Merging Government Food Agencies,' *The New York Times*, April 9, 1997, p.C1.
- 166 Caldwell Esselstyn, et al., 'A Strategy to Arrest and Reverse Coronary Artery Disease: A Five-Year Longitudinal Study ...,' *Journal of Family Practice* 41, no. 6 (December 1995): 560-68; Jane E. Brody, 'Huge Study of Diet Indicts Fat and Meat,' *The New York Times*, May 8, 1990, p.C1; Laura Shapiro, et. al., 'A New Menu to Heal the Heart,' *Newsweek*, July 30, 1990, pp.58- 59.

- 167 Gerry Oster, David Thompson, 'Estimated Effects of Reducing Dietary Saturated Fat Intake on the Incident and Cost of Coronary Heart Disease in the US,' *Journal of the American Dietetic Association* 96 (1996): 127-31.
- 168 'American Society of Primatologists Resolution on Organ Donation,' Source: Internet address, <http://www.asp.org/asp/resolutions/organ-donation>, November 6, 1996.
- 169 R. W. Evans, et al., 'The Potential Supply of Organ Donors: An Assessment of the Efficacy of Organ Procurement in the United States,' *JAMA* 267 (1992): 239-46.
- 170 Richard L. Worsnop, 'Organ Transplants: Can the Number of Donors Be Increased?,' *CQ Researcher* 5, no. 30 (August 11, 1995): 710.
- 171 L. Roels, et al., 'Effect of a Presumed Consent Law on Organ Retrieval in Belgium,' *Transplantation Proceedings* 22 (1990): 2078-2079.
- 172 M. F. X. Gnant, et al., 'The Impact of the Presumed Consent Law and a Decentralized Organ Procurement System on Organ Donation: Quadruplication in the Number of Organ Donors,' *Transplantation Proceedings* 23 (1991): 2685-2686.
- 173 Moussa Awuonda, 'Swedish Organ-Donation Drive Set For Success,' *The Lancet* 347 (May 18, 1996): 1401.
- 174 Aaron Spital, 'Consent for Organ Donation: Time for a Change,' *Clin Transplant* 7 (1993): 525-8; Aaron Spital, 'Mandated Choice: A Plan to Increase Public Commitment to Organ Donation,' *JAMA* 273 (1995): 504-6; L. G. Futterman, 'Presumed Consent ...,' *Am. J. Crit. Care* 5 (September 4, 1995): 383-8.
- 175 Lloyd Cohen, *Increasing the Supply of Transplant Organs: The Virtues of an Options Market* (Texas, R. G. Landes, 1995); Mike Wallace, narrating, 'Life By Transplant,' Sixty Minutes, November 26, 1995 and June 1, 1997, WCBS TV.
- 176 Reuters, 'Surgery Staves Off Heart Transplant,' March 17, 1997. Source: <http://www.yahoo.com/headlines/1970317/health/stories/>
- 177 Richard H. Hauboldt, (1996), p.26.
- 178 Richard H. Hauboldt, (1996), 32. At one institution, treatments for liver transplant patients cost between \$40,000 and \$50,000 for the first year of therapy and from \$6,000 to \$10,000 for each following year for the rest of the recipient's life. Karen Giuliano, 'Organ Transplants: Tackling the Tough Ethical Questions,' *Nursing* (May 1997): 38.
- 179 See M. E. Guinan, 'Estimating the Value of Preventing an HIV Infection,' *The American Journal of Preventive Medicine* 10 (1994): 1 - 4.
- 180 Richard H. Hauboldt, (1996), 1.
- 181 Robert E. Michler, (November 1, 1996).
- 182 United Network for Organ Sharing, *The Costs of Transplantation*, booklet, 1994, Richmond, Virginia.
- 183 Gina Kolata, 'Acrimony at Hearing on Revising Rules for Liver Transplants,' *The New York Times*, December 11, 1996, p.A20.
- 184 David Stipp, (November 25, 1996), 137; Anon, *The Economist*, October 21, 1995, p.83.
- 185 See, for example, T. Eastlund, 'Infectious Disease Transmission Through Cell, Tissue, and Organ Transplantation: ...,' *Cell Transplant* 4 (1995): 455-77; R. J. Simonds, 'HIV Transmission by Organ and Tissue Transplantation,' *AIDS* 7, Suppl. 2 (1993): S35-38.
- 186 Sam Seibert, Theresa Waldrop, 'Kidneys For Sale: The Issue is Tissue,' *Newsweek*, December 5, 1988, p.38.
- 187 Karen Giuliano, (May 1997): 36-7.
- 188 Gina Kolata, 'Controversy Erupts Over Organ Removals,' *The New York Times*, April 13, 1997, p.28.
- 189 Gina Kolata, 'When Death Begins,' *The New York Times*, April 20, 1997, Sec. 4, p.1.
- 190 Philip Keep, 'Transplant Lobby is Frightened to Face Facts,' *Hospital Doctor*, London, December 14, 1989, letters.
- 191 Mike Wallace, narrating, 'Not Quite Dead,' Sixty Minutes, April 13, 1997, WCBS TV.
- 192 Lawrence K. Altman, 'Doctors Treating AIDS Patient Turn to Baboon Marrow Cells,' *The New York Times*, December 15, 1995.
- 193 A. N. Warrens, et al., 'The Prospects for Xenotransplantation,' *The Quarterly Journal of Medicine* 89 (1996): 885-91; Charles D. Fulhage, 'Dead Animal Disposal Laws in Missouri,' May 1994, Source: <http://hermes.ecn.purdue.edu:8001/sgml/water-quality/missouri/wq216>, as of May 7, 1997.
- 194 Institute of Medicine, *Xenotransplantation: Science, Ethics, and Public Policy*, (Washington, DC: National Academy Press, 1996), 80.
- 195 R. W. Evans, *The National Cooperative Transplantation Study* (Executive summary), (BHARC-100-91-020 Control Number 01), Battelle Research Center, 1991.

- 196 David Stipp, (November 25, 1996); Franklin Hoke, 'Biotech Companies Set to Profit From Animal-Organ Transplants,' *The Scientist*, October 16, 1995, p.1.
- 197 Holly B. Brough, Allan B. Durning, 'Taking Stock: Animal Farming and the Environment,' Worldwatch Paper 103, July 1991, published by The Worldwatch Institute, Washington, DC. See also, Jeremy Rifkin, *Beyond Beef* (New York: Dutton, 1992).
- 198 National Geographic Society, 'National Forum on Nonpoint Source Pollution,' May 1995, cited in Jonathan Talbot, 'H-2 Oh My!' Source: <http://envirolink.org/arrs/AnimalLife/spring96/h20-my> as of May 7, 1997.
- 199 J. Warrick, P. Stith, 'Boss Hog: New Studies Show That Lagoons Are Leaking,' *The News and Observer*, Raleigh, North Carolina, February 19, 1995.
- 200 Ronald Smothers, New York Times News Service, 1995, cited in Jonathan Talbot, 'H-2 Oh My!' Source: <http://envirolink.org/arrs/AnimalLife/spring96/h20-my> as of May 7, 1997; Pamela Rice, reason #9 in '101 Reasons Why I'm a Vegetarian,' 1996 edition, published by The Viva-Veggie Society, New York.
- 201 Rodney Barker, *And the Waters Turned to Blood* (New York: Simon & Schuster, 1997); Linda Kanamine, 'Scientists Sound Red Alert Over Harmful Algae,' *USA Today*, November 11, 1996.
- 202 Kenneth F. Steele, ed., *Animal Waste and the Land-Water Interface*, Source: <http://www.crcpress.com/PRODS/L1189> as of May 7, 1997.
- 203 Charles D. Fulhage, 'Dead Animal Disposal Laws in Missouri,' May 1994, Source: <http://hermes.ecn.purdue.edu:8001/sgml/water-quality/missouri/wq216> as of May 7, 1997.
- 204 John M. Sweeten, 'Groundwater Quality Protection for Livestock Feeding Operations,' Source: <http://www.acesag.auburn.edu:70/0/waste-mgt/test-waste/fulldocs/animl-wst> as of May 7, 1997.
- 205 Natural Resources Defense Council, International Alliance for Sustainable Agriculture, *Hog Wash: Factory Farm Giveaways in Clean Water Act Proposals*, July 1995, p.4.
- 206 Ibid., p.2.
- 207 John M. Sweeten, <http://www.acesag.auburn.edu:70/0/waste-mgt/test-waste/fulldocs/animl-wst> as of May 7, 1997.
- 208 Richard Rhodes, 'Mad Cows and Americans,' *The Washington Post Magazine*, March 9, 1997, p.34.
- 209 Agricultural incinerators do not need permits to operate if they are burning Type 4 wastes which include animal remains, carcasses, organ and solid tissue wastes from farms, laboratories and animal pounds. Charles D. Fulhage, Source: <http://hermes.ecn.purdue.edu:8001/sgml/water-quality/missouri/wq216> as of May 7, 1997.
- 210 Researchers at Ridgetown College in Ontario claim that composting dead farm animals is "environmentally friendly." They recommend that compost sites face south where possible, be located on a well-drained site, preferably out of sight and a "suitable" distance from farms and neighboring residences. The compost unit can allegedly be located directly on a soil surface with drainage away from the site. A five foot wall should be built, they say, to keep scavengers out. Sawdust, corn cobs, or mixtures of manure, straw and "other materials" can also be used in the composting which takes nine months. Janice Murphy, 'New Regulations Allow Composting of Dead Stock,' *Pork News and Views*, March/April 1997, Source: <http://www.gov.on.ca/OMAFRA/english/llv...ews/>. The researchers do not explain, however, what materials may ooze from the site as the bodies decompose, where the leakage (which might include manure) would go, and what would happen in the event of a flood.
- 211 Charles D. Fulhage, as of May 7, 1997.
- 212 Claude E. Chastel, 'The Dilemma of Xenotransplantation,' *Emerging Infectious Diseases* 2, no. 2 (April-June 1996), letters.
- 213 Judith Reitman, 'Crossing Species: The Politics of Desperation,' *Mainstream* 27, no. 1 (Spring 1996), 21-22, published by the Animal Protection Institute, Sacramento, California.
- 214 David Foster, Associated Press 'Animal-Rights Tenets Are Gaining Support in U.S., Poll Shows,' *The Seattle Times*, December 3, 1995, p.A4; P. J. Mohacsi, et al., 'Aversion to Xenotransplantation,' *Nature* 378 (1995): 434. Results of a 1993 Gallup poll indicated that 50% of those questioned said they would accept an organ from an animal if a suitable human organ was not available. The Gallup Organization Inc., *The American Public's Attitudes Toward Organ Donation and Transplantation*, conducted for the Partnership for Organ Donation, Boston, 1993. This poll, however, was taken before the risks posed by xenotransplant procedures were publicly acknowledged.

Diseases Acquired From Non-Human Primates



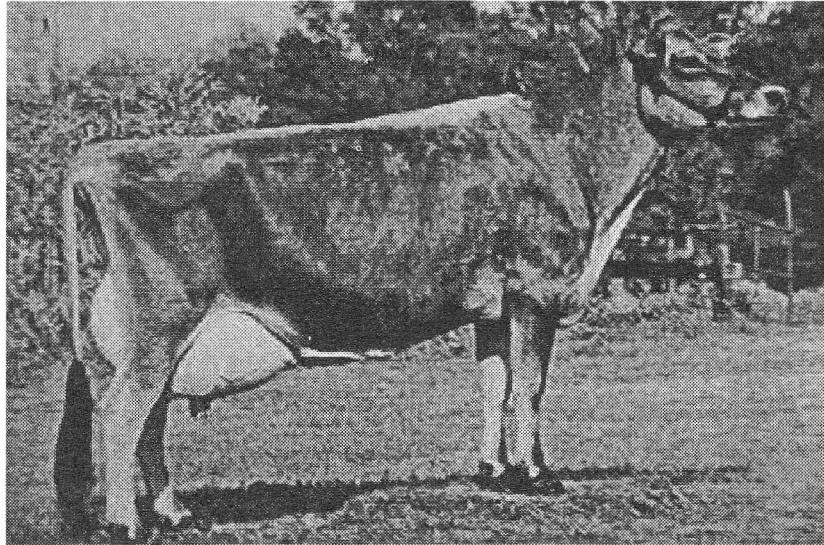
- Bertielliasis
- Campylobacteriosis
- *Entamoeba histolytica*
- *Entamoeba polecki*
- Giardiasis
- Hepatitis A
- Herpesvirus simiae (B virus)
- Herpesvirus tamarinus
- Leprosy
- Marburg virus
- Measles
- Monkeypox
- *Mycobacterium bovis*
- *Mycobacterium tuberculosis*
- Oesophagostomiasis
- Salmonellosis
- Shigellosis
- Simian immunodeficiency virus
- Tanapox
- Tularemia
- Yaba virus

Diseases Acquired From Pigs



- Anthrax
- *Ascaris suum*
- Botulism
- *Brucella suis*
- Cryptosporidiosis
- *Entamoeba polecki*
- *Erysipelothrix rhusiopathiae*
- Flavobacterium group IIb-like bacteria
- Influenza
- Leptospirosis
- *Pasteurella aerogenes*
- *Pasteurella multocida*
- Pigbel
- Rabies
- *Salmonella cholerae-suis*
- Salmonellosis
- Sarcosporidiosis
- Scabies
- *Streptococcus dysgalactiae* (group L)
- *Streptococcus milleri*
- *Streptococcus suis* type 2 (group R)
- Swine vesicular disease
- *Taenia solium*

Diseases Acquired From Cattle



- *Actinomyces pyogenes*
- Anthrax
- Brucellosis
- Campylobacteriosis
- Cowpox
- Cryptosporidiosis
- *Escherichia coli* O157:H7
- European tick-borne encephalitis
- Foot and mouth disease
- Giardiasis
- Leptospirosis
- *Mycobacterium bovis*
- Pseudocowpox
- Q-fever
- Rabies
- Salmonellosis
- Slow virus variant (?!? controversial)
- *Streptococcus zooepidemicus*
- *Taenia saginata*
- *Yersinia enterocolitica*

zoonosis

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PO Box 2751 Grand Central Station New York, NY 10163-2751
Tel: 212-832-3904 Fax: 216-283-6702 E-mail: mrmcmed@aol.com



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