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Welfare Issues with Genetic Engineering and Cloning of Farm Animals

The Humane Society of the United States

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An HSUS Report: Welfare Issues with Genetic Engineering and Cloning of Farm Animals

Abstract

Developments in biotechnology have raised new concerns about animal welfare, as farm animals now have their genomes modified (genetically engineered) or copied (cloned) to propagate certain traits useful to agribusiness, such as meat yield or feed conversion. These animals suffer from unusually high rates of birth defects, disabilities, and premature death.

Genetically engineering farm animals for greater bone strength or reduced pain reception, for example, may result in improved well-being, yet the broad use of this technology often causes increased suffering. The limited success of gene insertion techniques can result in genes failing to reach target cells and finishing in cells of unintended organs, and abnormally developed embryos may die *in utero*, be infertile, or born with development defects, attributable in part to insertional problems. Seemingly healthy genetically engineered farm animals may develop health concerns later in life, as a result of foreign genes lacking genetic controls, as evidenced by numerous studies. An additional concern with genetic engineering research lies in its low success rates. A research effort by the U.S. Department of Agriculture, for example, that modified the genes of dairy cows to produce more mastitis-resistant animals, resulted in a success rate of 1.5 percent: Of 330 attempts, only 8 calves were born, with 5 surviving to adulthood.

Recent cloning research also reveals high failure rates, premature deaths, and such abnormalities as intestinal blockages; diabetes; shortened tendons; deformed feet; weakened immune systems; dysfunctional hearts, brains, livers, and kidneys; respiratory distress; and circulatory problems. A 2003 review of cloning procedures in cattle found that less than 5 percent of all cloned embryos transferred into recipient cows survived, and a review published in 2005 confirmed that there has been no noticeable increase in efficiency. Surrogate mothers used in farm animal cloning research also suffer from reduced welfare from fetal overgrowth, repeated surgeries and injections, and pregnancy complications that have resulted in death.

Despite the low success rates and reduced animal welfare for surviving clones and surrogate mothers, the Food and Drug Administration's 2003 draft executive summary, *Animal Cloning: A Risk Assessment*, claimed that "the proportion of live, normal births appears to be increasing." However, members of the FDA's own Veterinary Medicine Advisory Committee felt that the agency had not adequately characterized the risk to animals and raised concerns about the level of animal suffering potentially caused by cloning. As recently as June 2005, an FDA representative stated that cloned animals were more likely to suffer birth defects and health problems when very young, demonstrating these problems have not been resolved.

In the United States, there are currently no regulations to protect the welfare of farm animals during cloning or genetic engineering agricultural research. This lack of oversight on what can be done to animals in pursuit of increasing agricultural output, coupled with the historical willingness of industrialized agriculture to sacrifice welfare for productivity, reveal many of the problems with much biotechnological animal research.

Background

Both the genetic engineering and cloning of animals involve the manipulation of DNA—the basic building block of all life. Genetic engineering involves the alteration of an animal's genetic information, including the addition (or "knock-in") and the removal or inactivation ("knock-out") of genes or their control sequences.(1) For example, the process of adding a growth hormone gene to increase growth rates involves isolating the gene and cloning it in bacteria to produce large quantities, before injecting the gene, under a microscope, into a pronucleus of a fertilized embryo flushed from his or her mother's oviduct. This embryo is then implanted into a surrogate mother who will give birth to offspring, some of whom will be transgenic—that is, containing the exogenous growth hormone gene in all of their cells.(2)

Clones are nearly exact genetic copies of an individual animal.* A recipient cell—usually an egg—is enucleated (all of its genetic information is removed) and the nucleus of a cell from the animal to be cloned (the donor animal) is inserted. Fusion of the recipient cell and the donor nucleus is initiated by electrical stimulation. Embryos produced by this nuclear transfer are then cultured in vitro for several cell divisions before being implanted into a surrogate mother.(3) The first animal successfully cloned from an adult cell, a sheep called Dolly, was born in 1996.

Researchers are genetically engineering and cloning farm animals for the food supply for a number of reasons, such as more profitable muscling and disease resistance. However, many applications of these technologies, particularly cloning, have been shown to be detrimental to animal welfare.

Genetic Engineering and Animal Welfare

While genetically engineering farm animals to increase bone strength or reduce reception to pain, for example, can improve animal well-being, the broad use of such technology generally does not result in a reduction of suffering. Gene insertion techniques have limited success, as inserted genes may fail to properly reach target cells and may finish in cells of unintended organs. Many embryos develop abnormally and die *in utero*, while others may be infertile or born with developmental defects, some of which are attributable to so-called insertional problems.(4)

Still other health issues may not become apparent until later in life. Transgenic animals often exhibit variable or uncontrolled expression of the inserted gene, resulting in illness and even death.(5) In one study, ten transgenic piglets were followed from birth through puberty, and half of the animals died or had to be euthanaized due to severe health problems during the investigation, indicating a high mortality rate among cloned piglets. In addition, three of the surviving piglets showed decreased cardiac output values.(6)

The genetic modification of sheep containing an extra copy of a growth hormone gene resulted in animals who grew faster, leaner, and larger than those conventionally bred or produced more wool or milk for prolonged periods. Developing more economically profitable sheep resulted in negative welfare side effects from the excess growth hormone, including increased incidences of diabetes and susceptibility to parasites.(7)

The transgenic "Beltsville pigs" had human growth hormone genes inserted in their genomes with the goal of increasing the animals' productivity. While that was partially achieved, the genetically modified animals suffered from numerous problems that severely compromised their welfare, including diarrhea, mammary development in males, lethargy, arthritis, lameness, skin and eye problems, loss of libido, disruption of estrous cycles, pneumonia,

* A cloned animal is not genetically identical to the animal from whom nuclear material was taken because of the very minor contribution of mitochondrial DNA from the egg.

pericarditis (inflammation of the sac surrounding the heart), and peptic ulcers. Of the 19 pigs expressing the transgene, 17 died within the first year.(8)

Similarly, a research effort by the U.S. Department of Agriculture modified the genes of dairy cows so the animals would be more resistant to mastitis, inflammation of the udder. Of 330 attempts, only 8 calves were born. Of those eight animals, only five survived to adulthood—a success rate of 1.5 percent.(9)

Cloning and Animal Welfare

Recent cloning research also reveals high failure rates and abnormalities, problems widely acknowledged by scientists in the field and indicative of poor animal welfare.(10,11) The list of problems from which clones can suffer is extensive, including enlarged tongues; malformed faces; intestinal blockages; diabetes; shortened tendons; deformed feet; weakened immune systems; dysfunctional hearts, brains, livers, and kidneys; respiratory distress; and circulatory problems.(12-16)

A 2003 review of cloning procedures found that while hundreds of calves have been cloned worldwide, less than 5 percent of all cloned embryos transferred into recipient cows have survived, and the majority of the 95 percent who did not survive died at various stages of development from a predictable pattern of placental and fetal abnormalities. “The low efficiency seriously limits commercial applicability and ethical acceptance of somatic cloning,” wrote the authors, “and enforces the development of improved cloning methods.”(17)

Two years later, a published review identified the challenges with cloning farm animals and confirmed there has been no noticeable increase in efficiency: “[A]t present it is an inefficient process: in cattle, only around 6% of the embryos transferred to the reproductive tracts of recipient cows result in healthy, long-term surviving clones. Of concern are the high losses throughout gestation, during birth and in the post-natal period through to adulthood. Many of the pregnancy losses relate to failure of the placenta to develop and function correctly. Placental dysfunction may also have an adverse influence on postnatal health.”(18)

Ian Wilmut, Ph.D., who led the team to clone Dolly the sheep, also found low success rates and a host of problems upon review of the world’s cloned animals. His review specified regularly occurring defects, such as fetal overgrowth, or large offspring syndrome, in cattle and sheep; heart defects in pigs; developmental difficulties, lung problems, and malfunctioning immune systems in cows, sheep, and pigs; and individual problems, including a lamb barely able to breathe due to grossly thickened muscles surrounding the lungs—which led him to conclude: “The widespread problems associated with clones has led to questions as to whether any clone was entirely normal….There is abundant evidence that cloning can and does go wrong….”(19)

The National Academy of Sciences acknowledged many of these problems in its 2002 report, *Animal Biotechnology: Science-Based Concerns*,(20) and the U.S. Food and Drug Administration also identified these issues during a 2001 hearing on cloning. Kathryn Zoon, a scientist with the FDA, testified before Congress that the failure rate remains extremely high for the cloned animals, and, when live births did occur, deaths and major abnormalities such as defective hearts, lungs, and immune systems have been documented. In addition, significant maternal safety risks—including deaths—have been observed.(21)

Despite the high level of inefficiency and recognized animal welfare concerns, the FDA’s draft executive summary, *Animal Cloning: A Risk Assessment*, claimed that “the proportion of live, normal births appears to be increasing.”(22) Members of the FDA’s own Veterinary Medicine Advisory Committee felt that the FDA had not properly characterized the risk to animals and were uneasy about the level of animal suffering a large cloning industry might cause.(23) In 2005, an FDA representative stated that cloned animals were more likely to suffer birth defects and health problems when very young.(24) Likewise, a January 2007 FDA report noted that perinatal calf and lamb clones have an increased risk of death and birth defects—demonstrating these problems have not been resolved.(25)

A recent, large-scale study of cloned sheep resulted in dramatic losses of lamb clones, all associated with placental abnormalities. Out of 93 attempts, only 12 clones reached full-term development. Of these 12, 3 lambs were delivered stillborn; 5 died of liver and kidney abnormalities within 24 hours of delivery by caesarian section; 2 died one day after birth from respiratory distress syndrome; and the remaining 2 lambs died at approximately four weeks due to a bacterial complication—a success rate of 0 percent.(26)

Cloning also threatens the welfare of surrogate mothers. According to cloning expert Mark Westhusin's testimony before Congress, of the cloned calves who do survive, most exhibit placental abnormalities that pose serious health risks not only to the developing fetus and offspring, but also to the surrogate mothers carrying the pregnancies, and have resulted in the deaths of both the fetuses and the surrogate mothers.(27) In addition, the birth weight of cloned calves may be 25-percent heavier than normal.(28) Fetal overgrowth, common to sheep and cattle clones, generally necessitates a caesarian section for the surrogates, an invasive surgery which, along with other intrusive reproductive procedures, can be performed repeatedly on the same animal.

In one cloning study, 4 out of 12 surrogate mothers died from pregnancy complications. According to Michael Bishop, Ph.D., of Infigen, a biotechnology company involved in cloning in the animal agriculture and human health arenas, such deaths still happen despite improvements in cloning. "We sacrifice the cow and the clone," he stated in a 2001 interview with *New Scientist*. "[A]ll the heroics in the world can't rescue those animals."(29)

Indeed, a Texas A&M University study of cloned transgenic calves resulted in 4 surrogate cows dying. Of the 13 fetuses studied, 5 were stillborn and 2 died after birth. One calf behaved normally at birth, only to die four days later. A necropsy revealed that the calf suffered from severe abnormalities: The animal's lungs had never properly developed, the heart was enlarged, and the liver, which should have been a smooth crimson organ, was a roughened orange slab.(30)

A Pew Initiative on Food and Biotechnology poll found that two-thirds of American consumers indicated that they are largely uncomfortable with animal cloning in general.(31) An earlier Gallup poll reportedly found that two-thirds considered animal cloning "morally wrong."(32)

Long-Term Welfare Problems

Biotechnology has produced a range of animals who sound like horrors from science fiction. Consider the so-called "legless mice," resulting from foreign DNA being inserted into the mice's chromosomes in a manner that altered an endogenous gene, resulting in a mutation. The first generation of mice produced by this procedure, known as insertional mutagenesis, appeared normal. However, when the transgenic mice were interbred, their progeny suffered severe abnormalities, including the loss of limbs, craniofacial malformations such as a cleft lip or cleft palate, and brain anomalies including highly aberrant or missing olfactory lobes. None of the mice survived for more than 24 hours after birth.(33)

Seemingly healthy bioengineered animals are at risk for a variety of defects. "All cloned babies have some sort of errors," stated researcher Ryuzo Yanagimachi. "I'm surprised they can survive it."(34) Another researcher, Rudolph Jaenisch, a biologist at Whitehead Institute at the Massachusetts Institute of Technology, reached a similar conclusion, stating, "Cloned animals that reach birth or beyond may appear normal, but our research shows they're not."(35) "From what we know, I would argue that cloned animals cannot be normal," Jaenisch concludes. "They can be closer to normal, but not normal."(36)

Some abnormalities may not show up until later in life. Particularly among cloned dairy cows, the most common causes of death are late-developing musculoskeletal problems so severe that the cows need to be euthanized. According to leading(37) cloning scientist David Norman Wells, the development of musculoskeletal problems, such as chronic lameness and severely contracted flexor tendons, in these high-production animals "emphasizes

the point that any underlying frailties in cloned animals may not be fully revealed until the animals are stressed in some manner."(38)

Immune deficiency is another defect challenging cloned animals. Researchers with the University of Missouri and the U.S. Department of Agriculture found the immune systems of cloned pigs do not fight diseases as effectively as those of non-cloned pigs. The cloned animals' immune systems did not produce sufficient quantities of natural proteins called cytokines, which animals must have in order to survive infections. This impaired immune function may contribute to cloned animals' susceptibility to illness and early death.(39)

Decreased immune function, combined with decreasing genetic diversity—a problem that will be exacerbated by even moderate adoption of cloning—increases vulnerability to disease. A single pathogen could devastate countless numbers of genetically identical animals, putting animal health and the global food supply at risk. The rampant spread of disease has already become an international problem and applying biotechnology to commercial animal agriculture could be disastrous in this regard.

The mounting evidence shows that death and deformities found in many cloned and genetically engineered animals are the norm rather than the exception, resulting in needless suffering.

Lack of Oversight

The federal Animal Welfare Act does not cover farm animals used in food and fiber research. The lack of regulatory or legal constraints on what can be done to animals in pursuit of increasing agricultural output, coupled with the historical willingness of industrialized agriculture to sacrifice animal welfare for productivity and profit, reveal many of the problems with much biotechnological animal research.(40)

While the U.S. Food and Drug Administration (FDA) is charged with regulating genetically engineered farm animals destined for the food supply under its New Animal Drug Authority (NADA), it has not yet developed regulations or public guidance that provide a clear determination of how the NADA process will apply to these animals. As NADAs are confidential by law, there may be no opportunity for prior public review of applications. The regulation of cloned animals is also under the FDA's jurisdiction. At present, the agency has yet to release for public comment its full risk assessment of cloning animals.(41)

On September 19, 2005, four days before his resignation, Lester Crawford, D.V.M., Ph.D., then Commissioner of the FDA, said in a speech before the 28th Annual National Food Policy Conference: "With respect to use of cloned animals for human food, FDA has stated upfront that the risk assessment methodology and all the information used in performing the risk assessment would be publicly available….Until the risk assessment is complete and publicly available, the *voluntary* moratorium on release of these products into the food supply remains in effect; and secondly, while our risk assessment only addresses the safety of food from animal clones and the risks to the cloned animals, *we are well aware that there are many social and ethical issues related to the cloning of animals*."(42) (Emphasis added.)

Indeed, while animal safety is part of the FDA's remit, it is clear that the agency's principal concern lies with food—not animal—safety. In fact, there are no regulations to protect the welfare of animals from dysgenic effects during cloning or genetic engineering.

Conclusion

High failure rates, defects, disabilities, and premature death of both surrogate mothers and offspring have plagued the application of biotechnology to farm animals. As there are currently no regulations to protect farm animals during cloning or genetic engineering in agricultural research, the welfare of these animals can and does suffer greatly.

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