Jeffrey Weinzweig's Experiments on In Utero Cleft Palate Repair in Goats (1999-2002) [1]

By: Kersten, Jillian R. Keywords: cleft palate [2]

Jeffrey Weinzweig and his team, in the US at the turn of the twenty-first century, performed a series of experiments on fetal goats to study the feasibility of repairing cleft palates on organisms still in the womb [3]. Weinzweig , a plastic surgeon who specialized in cleft palate repair, and his team developed a method to cause cleft palates in fetal goats that are similar to clefts that occur in human fetuses. Using their goat [4] congenital model, the team developed a method to repair a congenital cleft palate *in utero*, or in the womb [3]. The resultant goat [4] newborns had fully developed palates without scarring and with minimal functional impairment. The researchers recommended that surgeons use their repair methods in humans [5] to decrease the incidence of speech impairment commonly associated with cleft palate patients.

Weinzweig and his team performed a three part series of experiments on fetal goats at Weinzweig's laboratory at Brown University [6]'s Alpert Medical School in Providence, Rhode Island. The experiments took place over a three year period beginning in 1999 and ended in 2001. Weinzweig studied what he called the privileged window of fetal healing, when fetal tissue heals without scarring. Weinzweig aimed to see if a fully functional palate could be obtained by repairing the palate deformity *in utero*.

Weinzweig and his team in their first experiment in 1999 developed a method of inducing congenital cleft palates in fetal goats. Also in 1999, Weinzweig and his team demonstrated the feasibility of a cleft palate *in utero* repair in their second experiment. The third experiment in 2001, investigated the benefits gained through an *in utero* cleft palate repair and whether or not a fully functional palate could be obtained through an *in utero* cleft palate repair. Throughout the three part series of experiments, the Animal Research Facility at Brown University [6] provided veterinary care to the goats and the Poisonous Plant Research Laboratory analyzed and handled plant materials.

During human fetal development, the roof of the mouth, called the palate, forms between the eighth and twelfth weeks of gestation [7]. The palate has two parts, the hard palate, which is the bony front portion of the roof of the mouth, and the soft palate, the soft back portion of the roof of the mouth. A cleft palate or opening in the palate occurs when one or both portions of the palate fail to join properly during development. Weinzweig and his team developed a congenital animal model with similarities to the cleft palate condition in humans [5]. An accurate congenital model closely resembles the cause and development of a disease or abnormal condition in humans [5].

In this first experiment, Weinzweig used goats to model the fetal cleft palate. The team used sixteen pregnant goats, which yielded twenty-nine fetuses for study. To induce the development of a fetal cleft palate, the sixteen pregnant goats were exposed to anabasine, a chemical that can cause musculoskeletal malformations and cleft palates when consumed in large doses. The chemical was acquired from a plant slurry containing wild tree tobacco (*Nicotiana glauca* [8]), collected near Wikieup, Arizona. The *Nicotiana glauca* slurry, which inhibits fetal movement, was administered by Weinzweig's team into the pregnant goats' stomachs through a feeding tube twice a day, from gestational days thirty-two through forty-one, the corresponding time period during which fetal palate fusion along the mid-line occurs in goats. The pregnant goats were then euthanized and the fetuses were harvested for analysis and cleft measurements on days sixty, seventy, and eighty-five of gestation [7].

Using the Weinzweig team's protocol, twenty-eight out of twenty-nine goat [4] fetuses developed complete clefts of the hard palate and twenty-six out of twenty-eight of the clefts were bilateral, a cleft that extends to both the right and left sides of the palate. Additionally, all of the induced clefts were similar to each other in width and length. The clefts were also similar in form and structure to those found in humans [5].

The Weinzweig team postulated that their model could enable further study of craniofacial growth and palatal development. With ninety-seven percent occurrence of clefts, the team concluded that their method reliably produced cleft palates in goats. They published the protocol and results of their congenital model in February 1999.

Weinzweig and his team designed their second experiment to show the feasibility of an *in utero* cleft palate repair. Weinzweig's team employed their protocol to produce pregnant females that produced twelve goat [4] fetuses for the experiment. Weinzweig and his team performed *in utero* cleft palate surgical repairs on six of the twelve congenitally-clefted fetuses, while the remaining six congenitally clefted fetuses remained unrepaired to serve as a control group. On the eighty-fifth day of gestation [7], after the administration of anesthesia and prophylactic antibiotics, the researchers exposed a fetal goat [4] head through an incision made in the pregnant goat [4]'s abdomen and uterus [9]. With the fetal goat [4] head exposed, Weinzweig and his team surgically repaired the fetal goat [4]'s congenital cleft palates using a modified von Langenbeck technique, a surgical technique used in the surgical

repair of human cleft palates.

All twelve congenitally clefted fetuses were delivered alive at full term and survived the experimental intervention. Two weeks after their births, Weinzweig's team analyzed the newborn goats. The team's analyses showed no microscopic or visible scars in the congenitally induced clefts that were repaired *in utero*. The only sign of a cleft's previous existence was a slight indentation at the site of repair. When the goats reached six months of age, researchers reexamined the goats' repaired clefts. Their analysis showed normal palate development without scars.

During the six-month experimental period, all goats with congenital clefts repaired *in utero* could suckle and nurse without difficulty or assistance. The control goats with clefts struggled to nurse because the opening in the secondary palate did not allow for adequate suction in feeding. Three of the control goats also developed sinus and respiratory infections. This second set of experimental results demonstrated the technical feasibility of the first *in utero* repair of a congenital cleft palate model in some species. The results were published in October 1999.

Weinzweig's third experiment aimed to determine the possible benefits of *in utero* cleft repair in humans [5], and whether or not a fully functional palate could be obtained with fetal intervention of cleft palates. Weinzweig"s team again used their protocol to induce clefting of the palate in twelve fetal goats. Six of the twelve fetuses underwent *in utero* repair while the other six remained unrepaired as controls. Two unclefted goats were also used as controls. When the goats were six months old, Weinzweig's team placed a small flexible camera down the goats' nasal airways to see how the palates functioned. The goats were euthanized to remove the soft palate muscles, called velar muscles, from each goat [4]. The team then analyzed the harvested soft palate muscles using electron and light microscopy [10].

The Weinzweig team's analysis showed that the muscles of the palates functioned normally six months after *in utero* cleft repair. If a mammal [11]'s palate has inadequate muscular function, air escapes from the mouth through the nose, which leads to inappropriate nasal tones during vocalization and affects swallowing. In all *in utero* repaired clefts and unclefted control goats, Weinzweig's analysis showed strong contact between the soft palate and tongue, called velar motion, which produces sound. The unrepaired clefted goats did not show any velar motion or normal muscle function. Upon examining the tissue harvested from the goats, electron and light microscopic analyses showed atrophy of the soft palate muscle in the goats with unrepaired cleft palates, compared to the normal goats that served as a control. The soft palate muscles from goats with clefts repaired *in utero* were similar to those of the unclefted goats' muscles.

The experiments demonstrated the effects of *in utero* cleft palate repair. The Weinzweig team produced a fully functional palate without scarring. They said that this procedure could be applied in human cleft palate patients to decrease the incidence of speech impairment associated with cleft palate. They published their third set of results in June 2002.

Sources

1. Adzick, Scott, and Michael Longaker. "Animal Models for the Study of Fetal Tissue Repair." *Journal of Surgical Research* 3 (1991): 216–22.
2. Longaker, Michael, David Whitby, Scott Adzick, Leonard Kaban, and Michael Harrison. "Fetal Surgery for Cleft Lip: A Plea for Caution." *Plastic and Reconstructive Surgery* 6 (1991): 1087–92.
3. Perry, Ann. "Animal Scientist Finds New Vistas in Cleft Palate Research." *Agricultural Research* (2009): 4–6. http://www.ars.usda.gov/is/ar/archive/aug09/cleft0809.pdf [12] (Accessed November 8, 2015).
4. Weinzweig, Jeffrey, Kip Panter, Anthony Spangenberger, James Harper, Robert McRae, and Lee Edstrom. "The Fetal Cleft Palate: I. Characterization of a Congenital Model." *Plastic and Reconstructive Surgery* (1999): 419–28.
5. Weinzweig, Jeffrey, Kip Panter, Marcello Pantaloni, Anthony Spangenberger, James Harper, Felix Lui, Lynn James, and Lee Edstrom. "The Fetal Cleft Palate: II. Scarless Healing After *in utero* Repair of a Congenital Model." *Plastic and Reconstructive Surgery* 5 (1999): 1356–64.
6. Weinzweig, Jeffrey, Kip Panter, Anthony Spangenberger, James Harper, Robert McRae, and Lee Edstrom. "The Fetal Cleft Palate: III. Ultrastructural and Functional Analysis of Palatal Development Following *in utero* Repair of the Congenital Model." *Plastic and Reconstructive Surgery* 7 (2002): 2355–62.

Jeffrey Weinzweig and his team, in the US at the turn of the twenty-first century, performed a series of experiments on fetal goats to study the feasibility of repairing cleft palates on organisms still in the womb. Weinzweig , a plastic surgeon who specialized in cleft palate repair, and his team developed a method to cause cleft palates in fetal goats that are similar to clefts that occur in human fetuses. Using their goat congenital model, the team developed a method to repair a congenital cleft palate in utero, or in the womb. The resultant goat newborns had fully developed palates without scarring and with minimal functional impairment. The researchers recommended that surgeons use their repair methods in humans to decrease the incidence of speech impairment commonly associated with cleft palate patients.

Subject

Weinzweig, Jeffrey, 1963- [13] Fetal surgery [14] Fetus--Growth disorders [15] Diseases--Animal models [16] Animal models in

research [17] Brown University [18] Goats [19] Cleft Palate [20] Fetal Diseases [21] Maxillofacial Abnormalities [22] Orthognathic Surgical Procedures [23]

Topic

Experiments [24] Disorders [25]

Publisher

Arizona State University. School of Life Sciences. Center for Biology and Society. Embryo Project Encyclopedia.

Rights

Format

Articles [26]

Last Modified

Wednesday, July 4, 2018 - 04:40

DC Date

2017-04-06

DC Date Accessioned

Friday, April 7, 2017 - 17:52

DC Date Available

Friday, April 7, 2017 - 17:52

DC Date Created

2017-04-07

DC Date Created Standard

Friday, April 7, 2017 - 07:00

- Contact Us

- The Embryo Project at Arizona State University, 1711 South Rural Road, Tempe Arizona 85287, United States

---

Source URL: https://embryo.asu.edu/pages/jeffrey-weinzweigs-experiments-utero-cleft-palate-repair-goats-1999-2002

Links
[1] https://embryo.asu.edu/pages/jeffrey-weinzweigs-experiments-utero-cleft-palate-repair-goats-1999-2002
[2] https://embryo.asu.edu/keywords/cleft-palate
[3] https://embryo.asu.edu/search?text=womb
[4] https://embryo.asu.edu/search?text=goat
[5] https://embryo.asu.edu/search?text=humans
[6] https://embryo.asu.edu/search?text=Brown%20University
[7] https://embryo.asu.edu/search?text=gestation
[8] http://eol.org/pages/581054/overview
[9] https://embryo.asu.edu/search?text=uterus
[10] https://embryo.asu.edu/search?text=microscopy
[11] https://embryo.asu.edu/search?text=mammal
[12] http://www.ars.usda.gov/is/ar/archive/aug09/cleft0809.pdf
[13] https://embryo.asu.edu/library-congress-subject-headings/weinzweig-jeffrey-1963
[14] https://embryo.asu.edu/library-congress-subject-headings/fetal-surgery
[15] https://embryo.asu.edu/library-congress-subject-headings/fetus-growth-disorders
[16] https://embryo.asu.edu/library-congress-subject-headings/diseases-animal-models
[17] https://embryo.asu.edu/library-congress-subject-headings/animal-models-research
[18] https://embryo.asu.edu/library-congress-subject-headings/brown-university
[19] https://embryo.asu.edu/library-congress-subject-headings/goats

[20] https://embryo.asu.edu/medical-subject-headings/cleft-palate
[21] https://embryo.asu.edu/medical-subject-headings/fetal-diseases
[22] https://embryo.asu.edu/medical-subject-headings/maxillofacial-abnormalities
[23] https://embryo.asu.edu/medical-subject-headings/orthognathic-surgical-procedures
[24] https://embryo.asu.edu/topics/experiments
[25] https://embryo.asu.edu/topics/disorders
[26] https://embryo.asu.edu/formats/articles