NEWS ON DEVELOPMENTS
CURRENT DEVELOPMENTS AND ISSUES: A SUMMARY

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IN VITRO FERTILIZATION

Ovarian hyperstimulation syndrome occurs more frequently than generally acknowledged, IVF practitioners in a British hospital assert

Ovarian hyperstimulation syndrome (OHSS), a potentially fatal complication of ovarian stimulation regimens used for IVF and other assisted reproduction, "occurs more frequently than generally acknowledged," physicians from the IVF Unit at The Cromwell Hospital and The Royal Free Hospital in London write.

They report a case of severe OHSS in a 31-year-old woman that was successfully managed by aspiration of all visible follicles (there were 44), followed by IVF and cryopreservation of all normal looking embryos. Frozen-thawed embryos were inserted into the woman's womb in subsequent cycles. A viable pregnancy resulted on the second attempt.

NAZAR N. AMSO, KAMAL K. AHUJA, NORMAN MORRIS, and ROBERT W. SHAW. October 1989. Elective preembryo cryopreservation in ovarian hyperstimulation syndrome. *Journal of in Vitro Fertilization and Embryo Transfer.* 6(5):312–314.

Fertile woman, injected with GnRH agonist to treat husband's infertility, develops ovarian hyperstimulation syndrome

An IVF team from Brigham and Women's Hospital, Boston, Massachusetts, U.S.A., reports that a woman placed on leuprolide therapy prior to ovulation induction to improve ovarian response developed moderate ovarian hyperstimulation from the sole use of the GnRH agonist. They believe this to be the first reported case where the sole use of a GnRH agonist in a normally cycling patient resulted in such a syndrome.

The 32-year-old woman presenting for her second IVF attempt was apparently fertile. A complete evaluation of her revealed patent fallopian tubes and normal ovulatory cycles.

"Male factor was diagnosed as the cause of the couple's infertility, with the husband's semen analysis demonstrating both oligospermia . . . and decreased sperm motility . . . ," the team wrote.

The physicians observe that the management of a patient with ovarian hyperstimulation secondary to leuprolide therapy represents a dilemma.

"After 21 days of leuprolide administration, estradiol dropped to a castrate level in this patient, but the follicular cysts remained," they wrote. "A possible treatment in this situation is to puncture and aspirate the follicles. However, this is an unproved mode of treatment."

JOHN YEH, ROBERT L. BARBIERI, and VERONICA A. RAVNIKAR. August 1989. Ovarian hyperstimulation associated with the sole use of leuprolide for ovarian suppression. *Journal of in Vitro Fertilization and Embryo Transfer.* 6(4):261–263.

U.S. researchers experiment with microinjection of sperm, performing procedures on an apparently fertile woman

Researchers from the Fertility Institute of New Orleans in the United States report a case of egg fertilization by microinjection of human sperm from a man with obstructive azoospermia. This, they state, is the first report of microinjection of sperm aspirated from the caput epididymidis.

They describe their patient as a 47-year-old male with past proven fertility. He fathered two healthy and normal children by a previous marriage. His current wife, in whose body the microinjected egg was placed, is apparently fertile. The mother of one child, the 38-year-old woman is described as having regular menstrual cycles and a normal hysterosalpingogram.

So that the male patient could be treated, the fertile woman underwent controlled ovarian hyperstimulation, transvaginal ultrasound-guided aspiration of 13 eggs, and a laparoscopy (presumably under general anesthesia) for transfer of a microinjected egg into her fallopian tube.

"The patient did not conceive as a result of this transfer," the authors write. (While earlier in the report, the patient is described as the man, this term is now also used to describe the man's wife.)

The authors write: "Therefore, informed consent was given to microinject spermatozoa into the privitelline space of one-half of the oocytes in an attempt to achieve fertilization, while the remaining one-half were incubated in the original insemination medium." The authors do not state who gave the informed consent – the man, the woman, or both – or describe the nature of that informed consent, that is, what the man and woman were told about the status of microinjection, whether it was a treatment or an experiment, and what the chances were of a live, healthy birth resulting from the entire process.

T.T. OLAR, J. LANASA, R.P. DICKEY, S. N. TAYLOR, and DAVID N. CUROLE. June 1990. Fertilization of human oocytes by microinjection of human sperm aspirated from the caput epididymidis of an individual with obstructive azoospermia. *Journal of in Vitro Fertilization and Embryo Transfer.* 7(3): 160–164.

Fertile couples should be IVF candidates, Australian bioethics center maintains

Fertile couples should have access to IVF technology, according to the Centre for Human Bioethics at Monash University in Melbourne, Australia.

Existing legislation on IVF fails to take into account IVF's potential uses for fertile couples, senior researcher Dr. Karen Sawson said.

"Career women who leave their childbearing until late and women undergoing radiation treatment are at risk of having abnormal children," she explained. "Because radiation damages a woman's eggs, she could have them removed and stored as embryos before the treatment and implanted when she is well again. A woman leaving her child-bearing until her late 30s because of career choices has increased risk of abnormal children. In this case she could have eggs collected during her optimal age for childbearing, fertilised and stored for future transfer. This contributes to society by leaving the state free of providing services for genetically deformed children."

BLANCHE COOK. February 8, 1990. Give fertile IVF use – bio team. *Herald* (Australia).

U.S. physicians use IVF on fertile women in combination with electroejaculation machinery anally inserted into men to treat infertility in men who can not ejaculate

Physicians from the University of Michigan Medical Center describe their initial experience with electroejaculation and IVF in

seven couples in which the male is infertile due to the inability to ejaculate. The cause of anejaculation was spinal cord injury in six men and radical retroperitoneal lymph node dissection (RPLND) for testicular carcinoma in the seventh. Upon examination, all the female partners of the men were found to be in good health and without significant medical medical problems. All of the women demonstrated apparently normal pelvises.

The man with RPLND had normal sensation and needed general anesthesia for the electroejaculation procedure. Other men were sedated. Immediately before the electroejaculation, a catheterized urine specimen was tested for acidity and the bladder was washed out.

The physicians describe the electroejaculation: "A Model 10 electroejaculator probe . . . was inserted 6–8 in. into the anal canal with the patient in the lateral decubitus position. Progressively increasing voltage was delivered in a wavelike pattern until ejaculation was achieved. Stimulation was initiated at 2–3 V, with each subsequent stimulation occurring 608 sec later with an increase in voltage of 1 V. Blood pressure was monitored throughout the procedure . . . The antegrade sperm were collected by milking the phallus. After the procedure, the bladder was catheterized to collect the retrograde ejaculate. Five to ten ml of IUI medium was utilized to flush the bladder to obtain any residual ejaculate."

The authors point out that the effect of extended anejaculation on sperm production and function are not well known. They add:

"Moreover, the problem causing the anejaculation may result in other complications directly or indirectly affecting sperm quality such as chronic urinary tract infections in patients with spinal cord injuries."

Two pregnancies resulted from this series. One resulted in a live birth. The other ended in a 6-week spontaneous abortion. The authors conclude that while the number of patients involved in this series is too small to establish reliable success rates, the two pregnancies (one of which led to birth) demonstrate the potential of the technique.

JOHN F. RANDOLPH, JR., DANA A. OHL, CAROL J. BENNETT, JONATHAN W.T. AYERS, and ALAN C. MENGE. February 1990. Combined electroejaculation and in vitro fertilization in the evaluation and treatment of anejaculatory infertility. *Journal of in Vitro Fertilization and Embryo Transfer.* 7(1):58–62.

Fertile women, hired as "surrogate mothers" undergo embryo transfer in the United States

Physicians from the Mt. Sinai Medical Center of Cleveland in Ohio report the use of IVF on women with absent or dysfunctional uteri and the transfer of the resulting embryos into the wombs of women hired as surrogate mothers. To make this arrangement, the medical center worked with attorneys or agencies specializing in the procurement of women for reproductive purposes. The exact nature of the financial arrangement in effect with the hired women is not spelled out in the physicians' report in the *Journal of in Vitro Fertilization and Embryo Transfer.*

Six women with absent or dysfunctional uteri (each described in the report as an Ovum Donor or OD) consented to controlled ovarian stimulation, ovum aspiration, IVF, and embryo culture. Physicians transferred cleaving embryos to recipient women whose menstrual cycles were in approximate synchrony with those of the ODs. (The second category of women are referred to in the report as IVF-surrogates or IVF-S.) None of the IVF-Ss received medication.

Of the six reported cases, four led to full-term deliveries, one to an ongoing pregnancy, and one to a spontaneous miscarriage at 6 weeks.

The authors report: "Prior to initiating an active cycle, it was necessary to establish

ovarian asynchrony between the OD and the IVF-S. Both women were therefore instructed to maintain basal body temperature charts for at least one complete month prior to the active cycle."

Once these cycles were established, "oral contraceptives (OCs) were taken by the OD to suppress ovarian activity until the IVF-S began menstruation. Our clinical assumption was that if the OD would have had a functional uterus, menstruation could have been expected approximately three days after the cessation of the OCs. Therefore, when the OD stopped the OCs on the first day of menstruation of the surrogate ..." (Note: Quotation ends here as the point of including it is merely to give a sample of the language used in the report.)

LEON A. SHEEAN, JAMES M. GOLDFARB, ROBERT KIWI, and WULF H. UTIAN. June 1989. In vitro fertilization (IVF)-surrogacy: application of IVF to women without functional uteri. *Journal of in Vitro Fertilization and Embryo Transfer.* 6(3):134–137.

IVF used more on older women, and on fertile women married to infertile men

Women undergoing IVF are much older now and in 60% of the couples seeking help, the male has a fertility problem, according to U.S. IVF physicians Dr. Georgeanna Seegar Jones and Dr. Howard Jones, Jr. The Jones, who head the Jones Institute for Reproductive Medicine at the Eastern Virginia Medical School in Norfolk, Virginia, said that they were applying IVF to "a much more difficult population."

The average age of the clinic's patients has risen from 28 to 38, the Jones said.

Howard Jones said that "very heavy marketing by non-university programs" has caused "a certain discomfiture among patients who are becoming very conscious of asking what the pregnancy rate is. So, we have an era of consumerism that is different than we have experienced before and all of this has given rise to certain ethical questions which we have not faced before." (Those questions were not named in the newspaper report of Jones' remarks.)

Jones stated that IVF entrepreneurs were resorting to pregnancy claims "that cannot be substantiated."

SUE MILLER. June 18, 1989. More older women decide to try in vitro fertilization. *Register Guard* (Eugene, Oregon, U.S.A.).

Multiple births after IVF conceptions raise concerns

An Australian woman who gave birth to IVF quadruplets in early 1989 wants to have three of the four children adopted.

"It is believed the Perth woman, who wanted only one child when she sought in vitro fertilisation treatment, is under extreme emotional and some financial pressure since giving birth six months ago," Duncan Graham reported in *The Sunday Age.*

Before the birth of the quadruplets, she was already the mother of one child, also conceived following IVF.

Graham quotes Dr. Bruce Bellinge, the senior embryologist at the Concept IVF clinic where it is believed the woman was treated: "There is nothing to suggest that this girl is in trouble. Couples are fully counselled and aware of the financial and emotional costs (of treatment)."

Graham explained that because the IVF success rate is extremely low, there is pressure on doctors to implant more than one embryo in an attempt to improve that success rate. But one result of this is that multiple births are common in IVF.

In *The Australian,* Peter Terry reported that two of the quadruplets were already in foster care. Because they were underweight, they remained in Perth's King Edward Memorial Hospital from their birth April 24 until the first half of June. When the children eventually

came home, the parents hired a nanny. But after a week, they contacted a private foster agency. The two boys were taken into foster care, initially for a month.

In September, the West Australian government made an extraordinary cash offer in an attempt to persuade the parents of the quadruplets not to give up their children.

The Minister for Community Services, Mr. Smith, stated that he was prepared to offer the couple a cash sum and also to increase the $205-a-week federal and state assistance grants available to all parents after multiple births.

Smith stated: "I want to make it clear that in no way would I regard these payments as an end to the financial assistance that would be available in this particular case. Both in terms of ex gratia payments and special allowances, we will provide whatever is necessary to support the family in this situation."

New Idea reports the birth of another set of IVF quadruplets, this time to the young Melbourne couple Rob and Jenni Ramsey. All four babies died shortly after birth.

At 24 weeks of pregnancy, Ramsey went into labor and was admitted to the Monash Medical Center.

"Her uterus had become so stretched, she could no longer carry the babies," Diana Priestly reported.

After the death of the babies — Lara, Kirk, Jake, and Dylan—their mother Jenni Ramsay said: "The bottom fell out of my world. I felt a loss of control, direction and hope; a loss of my belief system. I felt I had failed the babies, my husband and myself. And it was a blow to my ego. For the first time in my life I was a fully functioning woman, then suddenly it was all over. It seemed so unfair. Why let me have children if I have to watch them die one by one?"

Ramsay has started infertility treatment again. She wears a computersied pump that releases hormones into her bloodstream every 90 minutes. She explains that the four dead children deserve a full-term living sibling and that for their sake, she would not give up the infertility treatments.

The month following its coverage of the Ramsey tragedy, *New Idea* ran a story on Cheryl and Bob Pavlenko, parents of the world's first PROST quintuplets. Under PROST–Pro-Nuclear Stage Transfer–six fertilized embryos were transferred from the laboratory to Pavlenko's fallopian tubes. She had had two previous IVF pregnancies following treatment at the Pivet Medical Centre in Perth, both of which miscarried. This time, five of the six embryos developed.

While the *New Idea* article describes Cheryl Pavlenko as "glowing with the radiance happiness brings" and states that "the quints have now filled the empty space in their [the Pavlenkos'] lives," most of the article focuses on Cheryl's extreme exhaustion and occasional desperation.

The Pavlenkos live with Cheryl's elderly parents in a small, now very crowded, house in the Perth suburb of Bedford. Pavlenko is reported as spending her entire day tending to the babies with never a moment to rest because there is always one or more baby crying for attention.

Pavlenko told reporter Jayne Newling: "I am exhausted and both Bob and I had no idea how hard it would be caring for five babies. They need constant attention and at the end of the day I am emotionally and physically drained. I feel burned-out sometimes. When they are all crying at the same time I get very upset. It's also very frustrating because every day there are piles of washing, bottles to be washed and sterilised, formulas to be made up and meals to cook now that they're on solid food."

Because of the constant demands on her, she does not feel like a normal person, Pavlenko told Newling. She said she felt more like a housekeeper than a mother. Referring to the friends and neighbors who come in during the day on a roster system to help care for the

babies, she said: "There are so many pairs of hands picking them up, cuddling them and feeding them, that I often wonder if they know who their real mother is. That makes me very sad."

She also said she felt very confined as she had only been able to manage three outings since the babies had been brought home – and two of those were visits to the hospital.

In an article on selective terminations in cases of multiple gestations, *Ob. Gyn News* reported on a presentation by Dr. Richard L. Berkowitz, director of the division of maternal-fetal medicine, Mount Sinai Medical Center, New York, U.S.A.

Injection of potassium chloride into the fetal circulation or heart has become the preferred approach to selective termination at Mount Sinai, Berkowitz reported.

The most common complications that occur while a physician is gaining expertise in selective abortion, he said, are "miscarriage of the entire pregnancy," or failure to cause asystole in a targeted fetus. Because of the potential for leaving a fetus impaired by the attempt to cause asystole, he explained, the termination procedure must be repeated.

Berkowitz noted that the first six twin pregnancies to undergo selective termination at Mount Sinai Hospital "worked out very badly," with the unintended miscarriage of four unaffected fetuses as well as the six targeted for abortion. These first attempts involved the use of exsanguination or injection of saline or an air embolism.

In general, he noted, the fetuses selected for reduction are those that are easiest to reach.

DIANA PRIESTLEY. August 19, 1989. The tragic side of IVF. *New Idea;* DUNCAN GRAHAM. September 10, 1989. Mother of IVF babies wants two adopted. *The Sunday Age;* PETER TERRY. September 16/17, 1989. WA offers cash to couple if they keep IVF quads. *The Australian:* p. 1; PETER TERRY and KEVIN RICKETTS. September 15, 1989. Mother wants to give up IVF babies. *The Australian;* JAYNE NEWLING. September 9, 1989. "If only I had five pairs of hands!" *New Idea:* pp. 4–7; *Ob. Gyn News.* August 1–14, 1989. Selective abortion in multiple gestation. 24(15):3.

Claims that we are witnessing an infertility epidemic challenged

The belief that infertility is increasing among women is probably more due to an increase in the number of office visits women make and the demand for fertility services among educated women that it is to a demonstrable rise in infertility due to delayed childbearing, Dr. Carolyn L. Westhoff said in New York.

Speaking at an undate on endocrinology and infertility presented by Columbia University College of Physicians and Surgeons, Dr. Westhoff of the university said: "We all have the impression that there is an epidemic of infertility going on out there, but I think a big piece of that [impression] comes from demand."

She challenged the perception that all women in their early and mid-thirties are at risk of infertility if they delayed childbearing. This perception grew out of a 1982 French report widely publicized in both the lay and scientific media. The report said that fertility in nulliparous women (women who have never given birth) drops from 74% before age 30 to 62% between ages 31 and 35 and to 54% by age 36. Many interpreted these results as being applicable to all women, regardless of parity.

The French study was embraced as definitive because it included only women undergoing artificial insemination by donor (AID), which excludes any fertility effects due to coital frequency or husband's age. Many physicians and patients concluded that a woman's chances of becoming pregnant drops sharply after age 30, Westoff said.

What many seemed to have overlooked, she pointed out, is that any nulliparous study group will contain many naturally sterile women and

that 12 cycles of AID are not strictly comparable with one year of intercourse, since intercourse typically results in much higher conception rates.

Data from the last cycle of the National Family Growth Survey contradict the dramatic drops in fertility reported by the French team, Westoff said. This data support earlier perceptions that infertility rises dramatically only during the late 30s and early 40s, she added.

Analyzing the data from 4,104 of the women in the Oxford (England) Family Planning Associates Contraceptive Cohort Study, Westoff also found that among parous women, age does not increase the risk of infertility significantly until after age 38.

The number of office visits made primarily for infertility now exceeds one million per year, about double the number reported two decades ago. This doubling appears to be due more to the increasing patient awareness of the availability of new reproductive technologies than it is to a rising infertility rate, Westhoff said.

Westhoff commented: "People used to think whether you got pregnant or whether you didn't get pregnant was just something you lived with. We now have a generation of reproductive-age people who have grown up with legal abortion, who grew up with the pill, and they've spent a large number of reproductive years [using contraceptives] and controlling their fertility. Now when they're ready to have a baby, they think they can control that too, and they're going to be much quicker to seek medical attention if they can't."

Ob. Gyn News. June 15–30, 1989. Infertility epidemic held artifact of high demand for fertility services. 24(12): 1.

More battles break out over control and ownership of frozen human embryos

A battle between an estranged husband and wife over the custody of seven human embryos ended in December 1989 when the couple agreed to donate the embryos to another infertile couple.

The embryos frozen in Melbourne, Australia's Royal Women's Hospital were the subject of a landmark custody dispute, the second such dispute in the world.

A Victorian husband and wife, each 24, had been enrolled in the hospital's IVF program prior to their separation. Earlier, the wife had been implanted with three embryos in the IVF program but the resulting triplets miscarried in the fifth month of pregnancy. The couple separated in March 1989.

According to legal sources, the woman wanted custody of the embryos so she could have them transferred to her uterus in an attempt to bear children. However, her estranged husband wanted to prevent her from doing so, fearing that he may be liable for maintenance of any resulting children.

In the first custody case of this kind, a Tennessee circuit court judge in the United States, Dale Young, awarded custody of seven frozen embryos to their biological mother, Mary Sue Davis, against the wishes of her estranged husband who did not want to become a father to any resulting children. (See: Estranged U.S. couple battle over seven human eggs fertilized in IVF program. *Issues in Reproductive and Genetic Engineering.* 3(1): 52-54.)

Commenting on the case before the out-of-court settlement, family law sources said the status given to the embryos would be a key factor in settling the dispute in Australia, Michael Pirrie reported in *The Age.* If an embryo is seen as a being, or a potential being, a judge may deal with the dispute as a custody case. If the embryos were awarded to a man, he could have the embryos implanted in a second wife or in a surrogate.

If the embryos are seen as property, like furniture, a judge might distribute them in a way he thought equitable.

But because the case was finally settled out of court, the legal status of frozen embryos is still uncertain.

The couple agreed to give the embryos to a donor program at Royal Women's Hospital where the embryos are being held. According to a report by Larry Schwartz in the *Sunday Age,* Dr. John McBain, a gynaecologist at the hospital, said legislation would ensure that the estranged couple would have no contact with their likely offspring. Nor would the people who received the embryos be told of their origin. So if children are born of the embryos, they will never know of the highly publicised controversy surrounding their conception.

If the woman had gained the embryos, Dr. McBain said, the hospital might have been placed in an awkward situation. It would have been "at odds with our stated policy," he said, to encourage the implantation only in couples who enjoyed a stable relationship and unlawful for implantation if the couple had been divorced at that stage.

According to a report in *The Sunday Herald,* this is not the first time in Australia that estranged couples have struggled over control of embryos frozen in IVF programs, but is merely the first time such a case has come to court.

Clem D'Alessandro, the Melbourne attorney acting for the husband in the current battle over the 13 frozen embryos, said he had "had a smattering of legal inquiries" over custody issues involving embryos but all had been settled out of court.

He said: "It's not the first time it's arisen. It stands to reason that with so many people on the IVF program these days, not all are happy marriages."

Another legal battle over control of frozen embryos is taking place in the United States. In this instance, one IVF clinic is refusing to allow a couple's frozen embryo to be transferred to another IVF clinic for implantation in the woman.

Risa and Steven York entered the IVF program operated by the Howard and Georgeanna Jones Institute for Reproductive Medicine in Norfolk, Virginia in 1986. Three IVF attempts there failed. When the Yorks moved from New Jersey to California in 1988, they asked the institute to ship their frozen embryo to an IVF program at Los Angeles' Good Samaritan Hospital, where Dr. Richard Marrs would supervise the transfer of the embryo.

Jones refused. He argued that the consent agreement signed by the Yorks gave them no rights to the embryo outside his institute's jurisdiction.

Time reported: "In effect, Jones contended, the Yorks have only four choices: they could have their embryo implanted at the institute, donate it to another couple, offer it for experimentation or destroy it."

In June 1989, a federal judge denied the Yorks' request for a preliminary injunction against the institute and ordered that the case be tried by a jury in the fall. This was a blow to the Yorks, who are worried that the passage of time will reduce their chances of having a child. Risa York is 39 and the spontaneous abortion rate for IVF increases dramatically in women beyond 40. Moreover, the longest recorded freezing of an embryo that was latter successfully implanted is 28 months; the Yorks' embryo has been frozen for 24 months.

MICHAEL PIRRIE. September 29, 1989. Court ruling expected to define when life begins. *The Age;* JULIE-ANNE DAVIES and JOHN GILLMAN. October 1, 1989. Frozen embryo battle may end in the courts. *The Sunday Herald;* LARRY SCHWARTZ. December 24, 1989. Children will never know they began as contested embryos. *Sunday Age;* AAP. December 28, 1989. Frozen embryos go to another couple. *Geelong Advertiser.* JOHN ELSON, MARY CRONIN, and FRANK FELDINGER. July 24, 1989. The rights of frozen embryos. *Time:* p. 63.

Ultrasound-guided transcervical tubal cannulation (TC-TEST) found less effective than IVF

An IVF team at PIVET Medical Center in Perth, Western Australia used ultrasound-guided transcervical tubal cannulation (TC-TEST) to place embryos in the fallopian tubes of 17 women whose tubes were inaccessible by the abdominal route. In each case, the women had at least one patent tube as shown in a hysterosalpingogram investigation.

In two further cases, physicians found it impossible to cannulate the tubes. In these cases and in two others where difficulty was experienced, a common feature was an arcuate or septate configuration of the uterus.

Three pregnancies (17%) occurred. The second pregnancy led to the birth of quadruplets at 31 weeks gestation. The authors state that the children are all healthy and thriving. The mother had had four previous failed IVF attempts and one failed TC-TEST attempt. The third pregnancy occurred in a 34-year-old woman who had a previous history of salpingectomy for ectopic pregnancy and was known to have partial agglutination of the fimbria of her remaining tube. Seven embryos were transferred to this tube, of which four were judged to be of good quality. Subsequent to the transfer, the woman suffered a tubal ectopic pregnancy. This necessitated salpingectomy of her remaining fallopian tube.

The investigators conclude: "The procedure has so far not shown a benefit over conventional IVF-ET and probably should be avoided in women with any type of tubal disorder."

JOHN L. YOVICH, ROGAN R. DRAPER, SIMON R. TURNER, and JAMES M. CUMMINS. June 1990. Transcervical tubal embryo-stage transfer (TC-TEST). *Journal of in Vitro Fertilization and Embryo Transfer.* 3:137–140.

Researchers suggest aspirating ovarian cysts before superovulation for IVF

Researchers from Texas propose that physicians may aspirate the ovarian cysts of women in IVF programs prior to superovulating the women with hormones. They base their proposal on their experience with three women. The women were found to have large ovarian cysts prior to undergoing ovarian hyperstimulation. Physicians aspirated the women's cysts transvaginally and then immediately began hyperstimulating their ovaries. All three women became pregnant following egg capture, IVF, and embryo transfer. In two cases, the pregnancies were ongoing. In the third case, the woman underwent dilation and curettage for a blighted ovum at 6 weeks' gestation.

The researchers note the common problem of an ovarian cyst encountered in the follicular phase of an IVF cycle. These cysts are most often noted after ovarian hyperstimulation in a previous cycle or recent treatment with a gonadotropin releasing hormone (GnRH) agonist. They point out that the reported incidence of persistent ovarian cysts is as high as 69% following nonconception clomiphene citrate (CC) cycles, with or without human chorionic gonadotropin (hCG); 56% following human menopausal gonadotropin (hMC)/HCG cycles; and up to 40% following GnRH agonist treatment.

Despite the common occurrence of these treatment-induced cysts, they comment, management of the cysts is controversial. Some physicians suggest avoiding ovarian hyperstimulation until the cyst resolves. Others recommend hyperstimulation of the ovaries despite the presence of a cyst. The authors present a third alternative: aspirating the cysts on the ovary and then immediately hyperstimulating the ovary.

The researchers noted that transvaginal aspiration of ovarian *follicles* did not gain widespread acceptance until 1984. While the safety of this procedure has been established, they continued, the safety of transvaginal aspiration of *cysts* remains controversial. In

the three cases they report, they did aspirate the cysts transvaginally under ultrasound guidance.

"If the cyst is malignant, the fear is that the diagnosis will be missed or that the malignant cells will be spilled into the peritoneal cavity, possibly leading to further spread of the cancer," they write. "This concern assumes importance because the reported incidence of ovarian carcinoma in infertility patients under the age of 40 is as high as 1.1 %."

After discussing the problem, they conclude that the risk of missing a malignant neoplasm is very low.

Advocating their method of cyst management, the researchers state that aspiration avoids delay of stimulation and offers the advantage of easier follicular monitoring during hyperstimulation. Additionally, in their three cases, aspiration did not interfere with immediate controlled ovarian hyperstimulation, subsequent egg capture, embryo transfer and pregnancy.

KAYLEN M. SILVERBERG, DAVTD L. OLIVE, and ROBERT S. SCHENKEN. June 1990. Ovarian cyst aspiration prior to initiating ovarian hyperstimulation for in vitro fertilization. *Journal of in Vitro Fertilization and Embryo Transfer.* 7(3): 153–156.

British Licensing Authority against sale of human eggs

"The sale of human eggs has been condemned by the Voluntary Licensing Authority [VLA], the body set up to monitor test-tube baby clinics and embryo research in Britain," *New Scientist* reports. "The reaction follows reports of clinics paying women for eggs or offering free sterilisation in return for egg donation," *New Scientist* states.

The VLA considers it unethical to try to induce women to donate eggs, such as the offer of free sterilisation. The VLA would like to make the sale of eggs a criminal offence. The VLA further reports that IVF pregnancy and birth rates have not really improved and that the rates differ from clinic to clinic. New clinics and smaller clinics usually have lower rates but even some of the established clinics have not had a pregnancy.

The VLA is not allowed to make public statistics from particular clinics and can thus not inform women of the best clinics for IVF. "The VLA said it was alarmed at the high rate of multiple pregnancies in women treated by GIFT," *New Scientist* reports. The rate for 1987 was 25%.

Sale of human eggs should be outlawed. *New Scientist:* May 27, 1989. p. 31.

Researchers use sperm to create transgenic animals

Researchers in Italy have taken mouse sperm and exposed them to foreign genetic material (DNA). The sperm seem to have picked up the new genetic material and carried it into mouse eggs that they fertilized.

If this experiment is repeatable by others it would revolutionize making transgenic animals. The usual method of placing new genetic material into animals is to inject the genes directly into the fertilized egg and then place the egg into a surrogate female. The method is labor-intensive and not very successful.

With the new method the mouse sperm seemed to pick up as many as 4000 copies each of the new gene into the head within a 15-minute period. The new gene was found in one-third of the offspring.

GAIL VINES. June 24, 1989. Sperm provides a bridge between species. *New Scientist:* p. 29.

EMBRYO RESEARCH

Embryo research to be banned in FRG

The government of the Federal Republic of Germany (FRG) has proposed legislation that would ban research on human embryos. The

new law would prohibit adding genes to human eggs, sperm, or embryos.

It bans cloning of humans, work with totipotent cells, research on human embryos that leads to their destruction and the formation of chimeras, or hybrids, between humans and other species. "If it is approved, the law will limit to five the number of embryos that geneticists can produce by in vitro fertilisation for a particular woman," *New Scientist* reports. "This is the maximum number that doctors will be allowed to implant into the woman after her eggs have been fertilised," *New Scientist* states. The doctors will be required to insert all in vitro embryos directly after they are produced.

Embryos may not be frozen, no research may be carried out on embryos that are stored currently in freezers, and embryos may not be created except for in vitro fertilisation.

The bill also would make it illegal to donate sperm and eggs and to use surrogacy. Prenatal diagnosis to determine the sex of the fetus would only be allowed in cases where a severe genetic disease might be inherited in that sex. Violation of the law could lead to 5 years of prison. "Hans Engelhard, the minister of justice, says that the mail purpose of the law is 'to exclude even the slightest chance for programmes aimed at so-called improvement of humans,'" *New Scientist* reports.

Scientists are critical of tie bill and say that it violates their constitutional right to "freedom of research" while the Greens don't think the bill goes far enough and would like to see a complete ban of IVF.

ROLF ZELL. July 29, 1989. Germany moves to outlaw embryo research. *New Scientist, p. 19.*

SURROGACY

Australian IVF physician challenges law forbidding surrogacy

The government of the Australian state, Victoria, has asked Parliament's infertility advisory committee to consider a request allowing a woman to act as a so-called "surrogate mother" for her sister. IVF physician Prof. John Leeton proposed this test case for Victoria's new IVF laws which place tight restrictions on surrogacy.

The married woman commissioning the arrangement is not infertile and neither is she childless. She has a 7-year-old son. It is asserted that she could risk death if she carried another child to term. She has had two miscarriages and gave birth to a still-born child last year. She wants her own eggs fertilized with her husband's sperm and inserted into her sister's uterus.

The woman told *The Sunday Herald:* "The baby will be ours. My sister will simply be the incubator. I don't see what is wrong with that."

Dr. Robyn Rowland, a social psychologist at Deakin University and a leading IVF critic, said that the request was an attempt by doctors to extend IVF procedures to new groups of fertile patients by highlighting difficult, emotional cases. These were intended to make it harder for politicians to refuse changes in the law, she said.

Commenting on a recent draft report by the National Bioethics Consultative Committee recommending that surrogacy laws be relaxed, Rowland said that it was "basically recommending that the Federal Government establishes a surrogacy agency where the Government controls, using women as breeders."

MARTIN DALY. December 17, 1989. Mothers the law rejects. *Sunday Herald* (Australia); MICHAEL PIRRTE. December 13, 1989. Woman wants IVF baby for her sister. *The Age.*

PREVENTABLE INFERTILITY

Cesarean section may increase women's risk of future infertility, study finds

Cesarean section may increase the risk of subsequent infertility, Dr. Alan S. Berkeley

said, in presenting the results of a study to a conference on perinatal care in San Rafael, California, U.S.A.

With colleague Dr. Anita Parnes La Sala, he evaluated the impact of cesarean section on fertility in 502 women who underwent primary c-section and an equal number of women matched for age and parity who had vaginal deliveries. The investigators had complete follow-up data of at least three years on 286 women in the study group and 268 in the control group.

Women in the study who underwent c-section were 18 times more likely to have a post-operative infection than those who delivered vaginally. About 28% of them developed endomyometritis and 9% developed another infection.

Those women in the study who were lost to postoperative fertility evaluation had a higher incidence of postoperative infection.

"So if those patients had been found and infection had anything to do with subsequent infertility, there should have been even more infertility in the c-section group," Berkeley, director of gynecology at New York Hospital, New York, said.

Reasons for infertility, such as Asher-man's syndrome, tubal factors, ovulatory dysfunction, and male factors, were found in very few of the women with infertility following c-section.

Berkeley offered the following explanation of why c-section affects fertility: It may be that many couples are marginally fertile, with such conditions as imperfect cervical mucus, inconsistent ovulation, a little scar tissue on the fallopian tubes, or borderline sperm counts. While these factors alone are not enough to make them infertile, the added insult of c-section, which can cause minor peritubal adhesions or intrauterine injury, throws them over a "fertility threshold" and makes them unable to conceive.

The finding of his study, Berkeley said, "probably won't affect obstetrics in New York, where malpractice premiums are in six figures, but if you're talking about the risk-benefit equation, I believe there is an infertility part to that equation. People don't worry much about it at the moment of delivery, but it's probably real."

Ob. Gyn News. June 15–30, 1989. Finds c-section may increase woman's future infertility risk. 24(12):3.

Physicians remove the uteri of one-third of U.S. women

If the current hysterectomy rate remains constant, about one in every three U.S. women will have a hysterectomy by age 60, Robert Pokras, a statistician with the National Center for Health Statistics, Hyattaville, Maryland, U.S.A., reported at a conference on women's health issues sponsored by Metropolitan Life Insurance Company.

Hysterectomy is second only to cesarean section among the most commonly performed major surgical procedures in the United States, Pokras said.

One trend in hysterectomy statistics, he reported, is an increasing rate of simultaneous bilateral oophorectomy (removal of both ovaries, i.e., castration).

Ob. Gyn News. June 15–30, 1989. 1 in 3 women will have hysterectomy by age 60, trends indicate. 24(12):7.

ABORTION

Abortion pill still having troubles

RU-486 is an antiprogesterone which can induce abortion when given in combination with prostaglandins before the 9th week of pregnancy.

It was developed by Roussel Uclaf in France and is now being used for 25% percent of all French abortions. It has a 96% success rate but there are no plans to market the drug internationally because antiabortion groups

have threatened to boycott the drug company and its partners.

Several countries are angry that the drug is being withheld for political rather than safety reasons, according to *New Scientist.*

Because the drug can only be given under the control of a doctor, women using the drug "should be able to claim reimbursement under the French social security system," *Nature* reports. Roussel Uclaf is charging the equivalent of 78 US dollars but the French health ministry will only pay 14 US dollars.

The health ministry states that the company can recoup the costs of developing the drug by selling it internationally. Since this is too sensitive at the moment, the company is looking for less controversial ways to use RU-486. One possibility is as a contraceptive.

New Scientist. July 29, 1989. Abortion pill withheld 'for political reasons', p. 19; PETER COLES. 1989. RU-486 still troubled. *Nature.* 340:6.

U.S. abortion ruling may extend state interest to entire pregnancy

The U.S. Supreme Court ruling "on the constitutionality of a Missouri law that places new restrictions on the right to an abortion appears to have sundered the connection between the legal view of abortion and the medical view of the course of pregnancy," *Nature* states.

"In so doing, it opens the door to a host of further legal cases that may both restrict further the availability of abortion and challenge biomedical practices in many other areas, from the use of in vitro fertilization to the treatment of fetal abnormalities," *Nature* reports.

The majority in the Supreme Court allowed a preamble in Missouri law that states that life begins at conception to stand. The preamble also states that 'unborn children have ... all the rights, privileges and immunities available to other persons, citizens and residents of this state," *Nature* reports.

Using the Missouri definition would not only forbid abortions but would also make certain types of contraceptives illegal, such as IUDs. Embryos created by in vitro fertilization would also be granted human rights and the destruction of excess embryos would be impossible.

ALUN ANDERSON. 1989. Abortion ruling divides the United States. *Nature.* 340:83.

GENETIC ENGINEERING

Human Genome Organization becomes international

The Human Genome Organization has decided to set up three regional offices, one at Osaka University in Japan, one at the Imperial Cancer Research Fund in London, England, and one at the U.S. National Institutes of Health, according to *Nature.*

The organization has 220 members representing 23 different countries. At a meeting in Geneva, HUGO asked "scientific funding agencies for money to pay for fellowships, scientific meetings, and to enable it to advise governments on the 'scientific, ethical, social, legal, and commercial implications' of genetic research," *New Scientist* reports.

However, Filippo Pandolfi, the EEC commissioner for science has "blocked the EECs programme on the human genome after protests from the European Parliament aimed largely at the technological implications of the research," *New Scientist* continues. Pandolfi is revising the proposals and wants them presented a second time to the European Parliament which will delay any decisions about money for HUGO. The delay raises fears that Europe will lose its chance to lead part of the human genome project to the US.

CAROL EZZELL. 1989. HUGO to go international. *Nature.* 339:3; p. 23. 1989. Genome's tortuous path. *New Scientist.* May 6.

Physical map of human genome possible within 5 years

The first step in mapping the human genome is to determine landmarks along the chromosomes at specific intervals. The second step is to create a physical map of where all the genes are on the 46 chromosomes using the landmarks. Then it will be possible to sequence the genes and thus sequence the entire genome.

Two new techniques have been developed that now make the first and second steps possible to complete within the next 5 years. Both techniques speed up the process of mapping considerably. "The map is certainly the project's most tangible goal, as it promises near-term benefits in tracking down the genes that cause major diseases such as cystic fibrosis and Huntington's disease," *Science* states.

The 5-year time span makes it more attractive to funders as well, such as the U.S. Congress.

LESLIE ROBERTS. 1989. Genome mapping goal now in reach. *Science.* 244:424–425.

Watson proposes "parcelling out" chromosomes

James Watson, director of the U.S. Human Genome Project, has proposed that an effective method "of mounting a mapping and sequencing effort might be to parcel out responsibility for collecting and collating information on specific chromosomes to different countries," *Science* reports.

Watson states, "The French might take several chromosomes and the Italians might take several others." The Soviet Union "might take a big chromosome," says Watson since the Soviet Academy of Sciences has allocated 40 million rubles to mapping genes.

Some are enthusiastic about the suggestion, especially the pharmaceutical industry, but many researchers are critical. Watson admits that the idea is more of a trial balloon to propose a possible model for international collaboration.

DAVID DICKSON. 1989. Watson floats a plan to carve up the genome. *Science.* 244: 521–522.

Symposium discusses impact of human genome project

A meeting called Human Genetic Information: Science, Law and Ethics was held in Bern, Switzerland at the beginning of July 1989. Organizers of the meeting were Ciba Foundation and the Academic Commission of the University of Bern, according to *New Scientist.*

James Watson, director of the U.S. Human Genome Project took up his proposal that different countries take different chromosomes while there. One result of the human genome project will be the identification of genes linked to specific diseases. It may also be possible to determine so-called "polygenic" diseases, diseases where scientists suspect that there is a genetic component, such as diabetes, heart disease, and cancer.

This kind of information raises legal and ethical questions. "Diana Brahms, a specialist in the law relating to medicine, said it might be possible in the future to identity people likely to develop a serious disease, long before the symptoms appear," *New Scientist* reports. This kind of information would be "'of considerable interest and value to any prospective employer, insurer, marriage partner or family member and would be of serious concern to the individual,' she said."

Discussion also turned to the use of genetic therapy, including manipulation of human sex cells and embryos. Most were sceptical to ideas of improving the human race by genetically engineering embryos but "Bernard Davies of Harvard Medical School said: Even if we find such uses trivial or repugnant, a world that accepts cosmetic surgery and the injection of silicone to enlarge breasts, and that

cannot prevent use of hormones by athletes, may find it difficult to limit nonmedical uses' of genetic manipulation if there is a market for them," *New Scientist* reports.

SHARON KINGMAN. July 8, 1989. Buried treasure in human genes. *New Scientist:* pp. 36–37.

Research proceeds on preimplantation diagnosis of genetic disease

Chicago scientists write in the *Journal of in Vitro Fertilization and Embryo Transfer* that there now exists a series of investigations preparatory to the possibility of preimplantation diagnosis of genetic diseases in human beings. These studies, the point out, are based on combining the existing technologies of artificial reproduction, micromanipulation, and genetic analysis.

It is proposed, they write, that mature follicles be aspirated from women at significant reproductive risk, that each oocyte or embryo undergo biopsy of either polar body, embryonic cells, or extraembryonic tissue, and that each biopsy be genetically analyzed.

They comment: "The technological aspects, micromanipulation of the embryo, incision of the zona pellucida, and excision of embryonic or trophectoderm tissue, are well-established procedures in animal models and have been successfully commercialized in animal husbandry practices. It, therefore, would appear likely that such procedures could be applied successfully to human cells/tissues, without undue cause for concern."

The scientists then ask:

- Whether there is any evidence to validate the idea that if a human oocyte or embryo is unknowingly damaged by the biopsy procedure, implantation would fail.
- Whether there is sufficient animal data on all the issues raised by the possibility of preimplantation diagnosis to consider the risks within acceptable limits and warrant approval for human experimentation.
- Whether there should be more extensive experimentation on primates.

They note that there may not be satisfactory answers to these questions but that the diagnosis of inherited characteristics in preimplantation embryos is nonetheless imminent. It may be that in time, they speculate, even pregnancies at risk because of advanced maternal age would be routinely offered preimplantation diagnosis.

YURY VERLINSKY, EUGENE PERGAMENT, and CHARLES STROM. February 1990. The preimplantation genetic diagnosis of genetic diseases. *Journal of in Vitro Fertilization and Embryo Transfer.* 7(1): 1–5.

National plan for genome project being developed

Researchers working in the U.S. Human Genome Project held a meeting in June to discuss progress with the project and to develop a national plan to lay before Congress.

James Watson stated that "Our immediate concern is to establish U.S. policy, which should be in place next spring. Of course we want to cooperate internationally, but all we can say is that we will cooperate when there is something to cooperate with," *Science* reports.

Fears have arisen that governmental red tape could stifle the attempts to build up international cooperation in the project. "The national plan will focus on overall goals of the program, its administrative and scientific organization, data handling, and ethical issues," *Science* states.

ROGER LEWIN. 1989. Genome planners fear avalanche of red tape. *Science.* 338: 1543.

Joint U.S.-British project to map nematode genome

The nematode genome is about the size of one human chromosome. Researchers in Great

Britain and the United States have been working on mapping the genome of the nematode and already have a rough physical map.

James Watson, director of the U.S. Human Genome Project, has proposed that these researchers be granted 600 000 U.S. dollars to then sequence the genome. This is expected to take 6 years for 50 technicians to accomplish. Sequencing this smaller genome is expected to function as a "stepping-stone" for the Human Genome Project.

CAROL EZZELL. 1989. The flatworm's turn. *Nature.* 339:648.

More U.S. agencies start genome projects

The Office of Human Genome Research at the National Institutes of Health will be reorganized and renamed as of October 1, 1989. It will then become the National Center for Human Genome Research.

This will allow the center to directly manage grant money instead of going through the office of the director of NIH. James Watson will become director of the center.

The Department of Energy and NIH also plan to meet to discuss the National Plan for the human genome project. According to Watson, both agencies are needed, "so that we can see the [genome project] not as DOE's assault on the genome and NIH's assault on the genome, but the nation's assault," *Science* reports.

The Department of Agriculture and the National Science Foundation have also decided to start genome projects. "The USDA already has an Office for Plant Genome Mapping Research," *Science* states. So far they have very little money but are hoping to receive more from USDA next year.

NSF is planning a workshop to discuss mapping the genome of a weed. *Arabidopsis thaliana.* This weed has a small genome which makes it possible to map and it is easy to grow in the lab. Some researchers are worried that the large sum of money that has been proposed for this project (35 million U.S. dollars) will drain financing of other important plant research.

Science states: "Politically, genome projects seem to have developed a life of their own. As an example, enthusiasm for the project at the Department of Health and Human Services prompted the department to raise NIH's original budget request for the genome project to nearly $62 million."

JOSEPH PALCA. 1989. Genome projects are growing like weeds. *Science.* 339:131.

Skin cancer gene search

Researchers in the U.S. think they have located a gene that causes malignant melanoma, a virulent form of skin cancer, to chromosome 1.

The search for the gene included the study of six families with a high incidence of the cancer. Only 10% of malignant melanoma cases are considered genetic.

The skin cancer rate is growing however, probably due to increased exposure to ultraviolet light. The researchers believe that as much as 50% of other skin cancer cases may also be linked to the gene. They have not found the actual gene yet, only a marker for it on the chromosome.

New Scientist. June 3, 1989. Search narrows for melanoma gene. p. 23.

Allergy gene found?

"Researchers at the Churchill Hospital in Oxford, England have located a single gene that predisposes people to allergy," *New Scientist* states.

The researchers used various standard tests for allergy on members of seven families with allergy problems. They also analyzed each family member's DNA using probes. One of these probes stuck to the DNA of those who had allergies indicating that this piece of DNA

was linked to an "allergy gene." This particular probe is specific for chromosome 11.

The researchers think the test could be used to find those newborn babies who are predisposed for allergy. Their families could "reduce the likelihood of allergies in their children by avoiding risk factors in the first few years of life," *New Scientist* reports.

Single gene may predispose people to allergy. *New Scientist.* June 24, 1989. p. 43.

Preimplantation diagnosis for cystic fibrosis

"Molecular biologists in East Germany [German Democratic Republic] and Britain, working with embryologists and gynaecologists, have shown that it is feasible to diagnose cystic fibrosis in very young embryos," *New Scientist* reports.

The researchers removed a cell from the embryo and used a technique called polymerase chain reaction (PCR) to make millions of copies of the DNA inside it. They then tested the DNA using a probe for the cystic fibrosis gene.

The method can only be used together with in vitro fertilization which has a very low success rate. "Yet, some couples who have had to terminate several pregnancies after prenatal diagnosis revealed that the fetuses were affected are asking for preimplantation diagnosis," *New Scientist* states.

Test detects cystic fibrosis in embryos. *New Scientist.* July 8, 1989. p. 39.

Amgen has problems marketing erythropoietin

Amgen Corporation has produced erythropoietin (EPO), a hormone that stimulates production of red blood cells, using genetically engineered bacteria.

The drug, called Epogen, is meant to treat the anemia that kidney patients on dialysis suffer from. Epogen has received approval from the Food and Drug Administration (FDA) in the United States for treatment of kidney patients.

Congress considers the drug to be too expensive however and is considering not reimbursing its costs via Medicare. The U.S. government decided that a previous genetically engineered drug, tissue plasminogen activator, was too expensive and would not be covered -by Medicare.

Amgen is having other problems with selling the drug as well. Epogen was developed under the Orphan Drug Act, which gives a 7-year monopoly to a company that develops a new drug that will have a very small market. This also affects the price of the product.

Amgen is also caught up in patent disputes with Genetics Institute and Chugai Pharmaceuticals. Amgen holds a patent for the EPO gene and the process for producing Epogen, but Genetics Institute owns a patent on human EPO, the product. Chugai is importing Japanese-made EPO to the United States. Amgen is also having a dispute with its marketing partner, Johnson & Johnson, over market shares.

ALUN ANDERSON. 1989. Growing pains for Amgen as epoetin wins US approval. *Nature.* 339:493.

"Human" insulin may not be diabetics' solution

"Preparations of 'human' insulin may put some insulin-dependent diabetics at life-threatening risk by depriving them of the warning symptoms of nypoglycaemia, a low level of sugar in the blood," *New Scientist* states.

"The rush among doctors over the past seven years to switch patients to the artificially produced human insulins, available in Britain since 1982, is the result mainly of promotional pressure from manufacturers, not a reflection of medical need, according to some researchers." A survey of 158 patients

who had been switched from beef or pig insulin to human insulin showed "that 53 percent felt that the control of blood sugar was worse and the warning of hypoglycaemia less clear," *New Scientist* reports.

According to Dr. Robert Tattersall at the University of Nottingham medical school, patients on insulin should be switched to human insulin only if they are allergic to animal insulin (which is rare) or if they don't respond to the animal insulin. Most patients don't need human insulin although many are being switched over to it. Some patients have been switched without being told by their doctors.

FRANK LESSER. April 15, 1989. 'Human' insulin loses its clean appeal. *New Scientist.* p. 30.

First genetically engineered vaccine against a parasite developed

"Researchers in New Zealand and Australia say they have developed the world's first effective vaccine against a parasitic disease using techniques of genetic engineering," *New Scientist* reports. Vaccines are normally only effective against viral and bacterial diseases.

The vaccine protects sheep from a tapeworm called *Taenia ovis.* The vaccine is expected to be on the market within two years and will save sheep farmers millions of dollars. The tapeworm makes the meat unusable and it has to be disposed of.

IAN ANDERSON. July 15, 1989. Tapeworm succumbs to engineered vaccine. *New Scientist,* p. 34.

First gene transfer experiment in humans takes place

The first gene transfer experiment in a human being took place in May in the United States. The patient received white blood cells that had been removed, infected with a marker gene, and then reinfused.

The cells are thought to attack cancer cells but researchers were not sure if they really sought out cancer cells. By using a genetic marker, they wanted to trace where the white blood cells went.

The test was given the go-ahead after a lawsuit filed by Jeremy Rifkin was settled. Rifkin did not intend to stop the experiment. His intent was to force the government to make the review process for future gene therapy experiments open to the public.

As part of the settlement in the lawsuit, the government's recombinant DNA advisory committee must include the public in its decision making.

BARBARA J. CULLITON. 1989. Gene test begins. *Science.* 244:913; CHRISTOPHER JOYCE. May 27, 1989. Treatment with genes creates medical history. *New Scientist,* p. 29; JOE PALCA. 1989. Go-ahead for gene transfer experiment. *Nature.* 339:243.

Rabies vaccine test stopped in United States

Researchers want to field test a genetically engineered rabies vaccine on South Carolina raccoons. The test site would be Cedar and Murphy Islands off the South Carolina coast.

The field test has been stopped by the South Carolina Health Department after passing through all the other regulatory steps. The health department wants more evidence of the vaccine's safety.

The vaccine has been developed by Philadelphia's Wistar Institute. Wistar got into hot water several years ago when they smuggled the vaccine into Argentina to test it on cattle. They never notified Argentinian authorities beforehand and the test created an international controversy when it leaked out.

To avoid bad publicity, Wistar hired a public relations firm to help but the effort backfired. Scientists at the health department found it irritating to get phone calls from influential people when they really wanted more data.

The vaccine is produced by Rhone Merieux, a French company. Rhone Merieux has stated that they would assume liability for the field test if something went wrong. However, their insurance policy had expired. "It's not the type of thing that builds confidence," one official stated to *Science.*

MARJORIE SUN. 1989. South Carolina blocks test of rabies vaccine. *Science.* 244: 1535.

New genetically engineered drug approved in Denmark

The Californian biotechnology firm Cetus has finally received approval of its drug interleukin-2 (IL-2). Denmark has approved the drug's use for renal cancer.

Cetus has been battling its competitor Hoffman-La Roche over patents for IL-2. The two companies have reached a cross-licensing agreement. The approval came at a time when Cetus was facing financial difficulties and it now hopes to pull itself out of its slump.

ROBERT BUDERI. 1989. Cetus banks on interleukin. *Nature.* 340:174.

Victorian Law Reform Commission supports research on human genetic engineering, despite opposition from leading IVF researcher

The Victorian Law Reform Commission recommended legislative changes to allow research into genetic engineering on human embryos in Victoria, despite opposition from IVF pioneer Dr. Alan Trounson.

In its report on genetic manipulation released in September 1989, the commission states that gene manipulation of human germ cells (eggs, sperm, or fertilised eggs) may be permissible in some circumstances and should not be legally prohibited.

Changes in human germ cells (for example, the insertion of extra genes into the chromosomes of human embryos for the purpose of eliminating genetic defects) can be passed on to future generations.

While many biologists argue that germ cell gene therapy is too experimental and, over many generations, could lead to catastrophic changes in the genetic character of the human population, the commission disagrees.

Germ cell gene therapy is prohibited indirectly in Victoria now by the Infertility (Medical Procedures) Act, which generally does not permit the use of IVF for the avoidance of genetic disorders. The commission wrote recently to the Victorian Standing Review and Advisory Committee on Infertility recommending a legislative amendment to permit IVF to be used to create an embryo for the purpose of preventing a genetic disorder.

Trounson, an IVF pioneer and head of the Centre for Early Human Development at Monash Medical Centre, said germ cell gene therapy was not yet possible in humans, but he believes it should be prohibited. He told science reporter Brett Wright: "It's something I feel very strongly about. We would prefer to see it completely out."

Trounson said similar experiments in animals had produced completely unexpected changes, such as tumours, structural deformities, and shortened life spans.

Wright reported: "He [Trounson] said the insertion of a new gene into human chromosomes could not be controlled and might lead either to changes which would worsen a patient's condition or produce serious genetic disorders which would only appear generations later. Dr. Trounson rejected the suggestion that further research could make germ cell gene therapy safe and doubted whether such techniques could ever be shown to be safe."

BRETT WRIGHT. September 17, 1989. IVF report sparks new debate. *Sunday Herald.*

Federal Republic of Germany prepares genetic engineering law

The Federal Republic of Germany's Health Ministry held a hearing in May 1989, to hear the responses of 25 interest groups to a law proposing to regulate genetic engineering.

The groups represented the environment, industry, unions, scientists, etc. Comments from these groups were used in drafting the version that the Cabinet later discussed.

At that point, the law proposal would have legalized the current regulations for genetic engineering. They included a monitoring organization (the Central Commission for Biological Safety or ZKBS), a rating system for work using pathogenic bacteria and rules for releasing genetically engineered organisms into the environment. Licensing would include input from the general public.

Researchers protested against the rating system for pathogenic bacteria and were pleased when the government dropped the licensing requirement for experiments with bacteria classified as "not dangerous." But scientific organizations still object to regulation of genetic engineering because they consider it no more dangerous than other methods of genetic modification.

The government cabinet approved the revised bill and it now goes to the Parliament for final approval, which is expected in the fall of 1990 with the bill taking effect in 1991.

In its present form the bill would require licensing based on different regulations for different types of genetic engineering projects: commercial, research, release into the environment, or confined use. The ZKBS will review applications and issue licenses except for deliberate releases, where other agencies will also be involved in the approval process.

In the case of deliberate releases, public hearings must be held before approval can be granted, but only when these "cannot be limited to a certain area," *New Scientist* states. The terms "confinement" and "area" are not defined which makes possible legal action to stop such releases. The law also "imposes liabilities on the experimenter for damages caused by genetic experiments, even if the authorities have approved the work, and even if the risk could not be foreseen at the time of approval," *New Scientist* reports.

ROLF ZELL and DEBORA MACKENZIE. July 22, 1989. Germany lays down the law on genes. *New Scientist,* p. 20; STEVEN DICKMAN. 1989. Germany edges towards law. *Nature.* 339:327; STEVEN DICKMAN. 1989. West Germany eases law. *Nature.* 340:85.

German law sends industry running

Biotechnology companies in the Federal Republic of Germany are moving factories to other countries where the regulations on genetic engineering are not as stringent.

BASF is planning to open a biotech laboratory in Boston, Massachusetts and Bayer is planning to build a biotech factory in Berkeley, California. The companies are fleeing because of legislation making it mandatory that all proposals for new factories be debated publically.

"The debate over biotechnology has been influenced by a growing public dismay over Chernobyl, the Bhopal accident and last year's major chemical spill in the Rhine," *Science* reports. "This has led to public cynicism regarding official statements about the safety of such technologies. 'Some people feel that they cannot always trust the scientist,'" as Ernst-Guber Afting of Hoechst put it in *Science.*

DAVID DICKSON. 1989. German biotech firms flee regulatory climate. *Science.* 244: 1251–1252.

Royal Commission and Department of Environment propose laws in Britain

In anticipation of a long-awaited report from the Royal Commission on Environmental Pollution (RCEP), the U.K. Department of the Environment (DOE) has proposed legislation

on deliberate release of genetically engineered organisms.

The DOE proposes that all deliberate releases must obtain approval from the DOE and that the cost of the consent process be borne by the applicant. DOE suggests that a register be set up for all applications that would be open for public scrutiny.

The RCEP report was published a few weeks after the DOE proposal. According to the report, the RCEP proposal would make deliberate release without a license a criminal offence. The commission argues that there may be risks with deliberate release of genetically engineered organisms into the environment. Thus they suggest that such experiments should be scrutinized by experts and be licensed by the Secretary of State for the Environment and the Health and Safety Commission.

The RCEE recommends three levels of monitoring. "The first is inspection of laboratories, production plant and test sites," *New Scientist* reports. The second level would be monitoring of the environment and the effect the released organisms have on ecosystems. The third level would require that the releasers, "should monitor the fate of their products," *New Scientist* states.

The RCEP also voiced concern about using retroviruses for transferring genes since they may inadvertently pass them on to other species. They also think it inappropriate to use antibiotic markers for monitoring the movement of organisms as this may increase the risk of spreading antibiotic resistance to organisms in the environment.

PETER NEWMARK. 1989. UK. law in the offing. *Nature.* 339:499; PETER NEWMARK. 1989. Controls needed on release. *Nature.* 340:84; SUSAN WATTS. July 15, 1989. Genes at the bottom of the garden. *New Scientist.* pp.31–32.

Denmark eases law on deliberate release

The Danish Minister of Environment, Lone Dybkjaer, has granted approval for the first deliberate releases of genetically engineered organisms in Denmark.

The field trials will test two types of sugar beets, one with an herbicide resistance gene and the other with a virus resistance gene. Three Danish companies – Danisco, Novo-Nordisk and Carlsberg – are relieved at the decision. Denmark is the only European country with legislation restricting such releases.

Other rules have also been relaxed. Pilot plants will be treated as research facilities, which means they do not have to follow the stringent guidelines for production facilities. Companies no longer have to stop working when a complaint is made to the Environmental Appeal Board as well.

Danisco, a food conglomerate, is the company behind the sugar beets. They will be tested during 1990. The herbicide resistant beet has been made to resist Monsanto's herbicide Roundup.

PETER NEWMARK. 1989. Danish law to be less rigid. *Nature.* 339:653.

U.S. to finalize genetic engineering regulations

A final draft proposal of regulations for the release of genetically engineered microorganisms into the environment is to be approved soon. The regulations will fall under laws that already exist including the Toxic Substances Control Act.

The focus of attention will be on the product itself and not on the process used to produce it. The Environment Protection Agency (EPA) will be given jurisdiction over all new genetically engineered microorganisms. Over 50 applications have been submitted to field test microorganisms and the EPA has approved 10 of them.

New Scientist. July 15, 1989. US. finalises controls on genetic engineers, p. 29.

European Patent Office says no to oncomouse patent

The European Patent Office (EPO) rejected a patent application for a genetically engineered mouse, the so-called oncomouse.

The mouse is engineered to develop a human type of cancer and has been given a patent by the U.S. Patent Office. The EPO interprets the European Patent Convention as prohibiting the patenting of animals or plants. The decision will be appealed by the applicants – Harvard University and Du-Pont.

This decision will add fuel to the debate on patenting as the European Commission has sent out a proposal to allow patenting of animals and plants produced by genetic engineering.

DAVID DICKSON. 1989. Europe says no to animal patents. *Science.* 245:25; p. 20; 1989. Europe shuns transgenic animals. *New Scientist.* July 8, STEVEN DICKMAN. 1989. Oncomouse seeks European protection. *Nature.* 340:85.

Genetically engineered petunias to be field tested in FRG

"Forty thousand genetically-engineered pink petunias are to bloom in West Germany [Federal Republic of Germany] despite the continuing controversy over new legislation to control such experiments," *Nature* reports. The petunias will probably be planted during 1990.

STEVEN DICKMAN. 1989. The flowers that bloom next spring. *Nature.* 339:325.

Genetic erosion and the coming change in climate

The greenhouse effect will lead to climate changes which in turn will affect the plants that can be grown in different parts of the world.

The world depends on 30 plant species for over 95% of its food, but these hybrid varieties may not survive the predicted climate changes. The genetic variation needed to adapt or improve these plants is fast disappearing because of genetic erosion – the extinction of varieties and species of plants.

Genetic erosion is man-made. Industrialization destroys the environment and many plant's habitats. Modern agriculture and plant breeding have reduced the variety of crop types available, leading to the loss of local varieties and their unique genetic characteristics.

Wars have ravaged areas of Afghanistan, for example, where varieties of wheat specially adapted to the climate there were cultivated. Even gene banks are not a guarantee that genetic variation in plants will be saved. Of 250,000 plant species, only 5,000 have been studied to some extent which means that scientists know little about which plants to save.

OMAR SATTUR. July 29, 1989. The shrinking gene pool. *New Scientist,* pp. 37–41.

Danish biotechnology companies merge, market engineered enzyme

The two largest pharmaceutical companies in Denmark, Novo Industri and Nordisk Gentofte, have merged to form the new company Novo-Nordisk.

The two companies combine their expertise in hormone production using genetic engineering techniques and production of industrial enzymes, according to *Nature.*

One of Novo-Nordisk's latest products is a detergent containing a fat-dissolving enzyme produced by genetic engineering. *New Scientist* reports that the enzyme, Lipolase, is produced by splicing a gene from one type of fungus into another that can produce it in large quantities. The detergent has been tested in Japan and plans are underway to introduce the enzyme in European detergents.

P.N. 1989. Danish merger. *Nature.* 339:5; SUSAN WATTS. July 1, 1989. Engineered

enzyme washes whiter than white. *New Scientist,* p. 45.

DNA fingerprinting on trial

A double murder trial in the United States has called into question the accuracy of DNA fingerprints used as evidence. In its wake it has also called into question numerous convictions based on DNA analysis performed by two companies, Cellmark Diagnostics of Maryland and Lifecodes of New York.

The defence and the prosecution attorneys in the murder trial assembled some of the leading molecular biologists as witnesses in a Frye hearing, a pre-trial hearing to determine if the evidence is admissible.

The scientists for both sides were afraid the scientific complexities of the method would not be made clear in a trial. So they decided to band together and scrutinize the data without the lawyers. Together they prepared a consensus document that found no fault with the method when properly done, but found the evidence in this case to be terribly flawed.

Lifecodes analyzed blood found on the watch of the murder suspect and supposedly found it to match the victim's blood. But the scientists raised the question of inadequate controls in the analysis and the lack of standards in how the test was performed and how the data was interpreted.

Contamination could not be ruled out as a cause of some of the bands in the fingerprints. The conclusion of the group was that the evidence in this case was not scientifically reliable and if it had been sent to a peer-reviewed journal it would never have been accepted. They call for a set of guidelines for DNA fingerprinting in forensics.

The judge will have to make a ruling on whether the DNA analysis is admissible as evidence, but has also been asked to make a ruling on whether such evidence is admissible in general. It is expected that the DNA analysis made by Lifecodes will be thrown out, but many see a general ruling as being premature.

The Office of Technology Assessment and the National Academy of Sciences are both looking into the scientific validity of the method and it is expected that their reports will be necessary for such a judgement.

CHRISTOPHER JOYCE. May 6, 1989. The finger of doubt points at "foolproof" fingerprinting. *New Scientist,* p. 24; MARCIA BARTNAGA. 1989. Pitfalls come to light. *Nature.* 339:89; ROGER LEWIN. 1989. DNA typing on the witness stand. *Science.* 244:1033–1035; ALUN ANDERSON. 1989. New technique on trial. *Nature.* 339:408; ERIC S. LANDER. 1989. DNA fingerprinting on trial. *Nature.* 339:501–505; ROGER LEWIN. 1989. DNA typing is called flawed. *Science.* 245: 355.

DNA tests approved for official use in Great Britain

DNA analysis or fingerprinting has been added to the list of methods that the British courts can request be used in paternity cases. A similar plan will be approved shortly for immigration cases.

The method has previously been accepted by the government for use in immigration cases and has been performed by Cellmark Diagnostics. No one has discussed the quality of the analyses used as evidence as yet. The Home Office plans to monitor laboratories wanting to perform the tests, although no licensing system exists.

CHRISTINE MCGOURTY. 1989. Genetic tests made official by UK courts. *Nature.* 339:408.

Caution urged with DNA fingerprinting in behavioral ecology

The method of DNA fingerprinting can be used to identify individuals and determine their relatedness to other individuals, something the test has been used for in forensics and by immigration authorities. The method can also be used by biologists to study the individuals in an animal population.

Behavioral ecologists have seen DNA fingerprinting as a revolutionary tool to study reproductive success in wild populations. Which individuals mate and leave the most progeny is an important variable in reproductive success and biologists are interested in learning more about what types of behavior enhance this success.

But to study such questions it is crucial to identify which individuals have produced which offspring. DNA fingerprinting was hoped to identify which individuals were related to each other and how. But studies in several species have shown that unrelated individuals can have as much as 40% of their DNA fingerprint in common, just by chance.

This noise in the system may make the method much less usable than biologists supposed and many are voicing that caution should be used when drawing conclusions based on the method.

ROGER LEWIN. 1989. Limits to DNA fingerprinting. *Science.* 243:1549–1551.

National DNA fingerprint register planned in Great Britain

"A national register of DNA profiles may be created within 2 to 5 years, according to the British government's Home Office," *Nature* reports.

The profiles would be stored in a computerized database. By the time the database is ready the government hopes to have dealt with the legal and ethical questions that it will raise.

One of these is the question of consent before a sample for a DNA fingerprint can be taken. Currently an individual must give consent for such a sample to be taken but there is pressure to change the law to make it "a legal requirement to provide a sample for a DNA test."

CHRISTINE MCGOURTY. 1989. Profiles bank on the way. *Nature.* 339:327.

India offers cheap DNA fingerprinting

"The Centre for Cellular and Molecular Biology (CCMB), an Indian government laboratory in Hyderabad, hopes to provide DNA fingerprinting services to customers in India and abroad at a price much cheaper than the fees currently charged for similar service by British and American companies," *Nature* reports.

The director of CCMB, Dr. Pushpa Bhargava, hopes that the low cost of the method in India will make its services attractive internationally.

K.S.J. 1989. Cut-price fingerprints. *Nature.* 340:175.

Cancer deaths at Pasteur Institute investigated

Willem Roskam was the seventh researcher who had worked at the Pasteur Institute to develop a rare form of cancer.

All seven "worked on the same floor, at about the same time and all had been involved with research using recombinant DNA," *Nature* reports. Roskam is the fourth to die of cancer.

"By 1986, five cases of cancer had developed and by 1987 the number had risen to seven," *Nature* continues. "We began to ask ourselves some questions', says Maxime Schwartz, director of the Pasteur Institute." The Institute has initiated an epidemiological study of present and former employees and has sent out questionnaires to more than 4,000 people.

"If the inquiry indicates a link between the cancers and the victims' occupation, says Schwartz, the problem may well turn out to apply elsewhere," *Nature* states.

PETER COLES. 1989. Inquiry into Pasteur deaths. *Nature.* 338:607.

Students protest microbiologist's research

Fifty students from the University of Massachusetts were arrested in April 1989,

after occupying a university building in protest of microbiologist Curtis B. Thorne's research.

Thorne's research on anthrax is funded by the Army's Biological Defense Research Program. The occupation caused the Amherst Board of Health to discuss banning "the testing, storage, transportation and disposal of biological materials if funded in full or in any part by the U.S. Army's Biological Defence Research Program," *Nature* reports.

Supporting Thorne, the chancellor of the university stated that he would protect the right of scientists at the university to conduct research as long as it was open to public scrutiny. Several molecular biologists however stated that Thome's research was a threat to community health and "could not be construed as for peaceful purposes," *Nature* states.

SETH SHULMAN. 1989. Microbiologist butt of protests. *Nature.* 339:6.

"Gene shears" to be marketed in Australia

"Gene shears" are one of the latest tools in genetic engineering. The technology is based on strands of RNA which can find and stick to specific strands of mRNA and then cut them up so they no longer are active.

mRNA is a copy of a gene that is used by the cell to produce whatever the gene codes for. If the mRNA is destroyed, the gene is silenced and what it codes for is never produced.

Gene shears are specially designed strands of RNA that can cut specific mRNA to silence a particular gene and can thus be used to produce changes in plants and animals. The method was developed by Australia's national research organization, the CSIRO, which has signed an agreement with the international seed company Groupe Limagrain from France.

The two have created a new company called Gene Shears in Canberra and they plan to develop gene shears that inactivate viruses that attack plants.

GRAEME O'NEILL. July 29, 1989. Genetic 'shears' cut their way to market. *New Scientist,* p. 33.

Glow-in-the-dark bacteria developed

Bacteria which have been genetically engineered to contain the gene for luciferase, a firefly enzyme will glow when supplied with the enzyme's substrate, luciferin.

Several different species of insects are bio-luminescent but emit different colors. Researchers at the University of California in San Diego transferred genes from click beetles to the bacteria *E. coli* and found bacteria that glowed with one of four different colors. The researchers hope to use the genes as genetic markers.

JEREMY CHERFAS. June 24, 1989. Firefly factor makes colourful genetic marker. *New Scientist,* p. 45.