THE EVOLUTION OF IN VITRO FERTILIZATION IN THE UNITED STATES: A CLOSER LOOK AT MEDIA COVERAGE

Jillian Clair Canada

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Approved by
Advisor: Chris Roush
Reader: Jan Yopp
Reader: Dr. Stan Beyler

ABSTRACT

JILLIAN CLAIR CANADA: The Evolution of In Vitro Fertilization in the United States: A Closer Look at Media Coverage

(Under the direction of Chris Roush, Jan Yopp and Dr. Stan Beyler)

Since the inception of in vitro fertilization in the United States in 1981 the U.S. media have covered its advances, moral debates and oddities. The reproductive technology, which manually combines both egg and sperm to form an embryo outside of a woman's uterus, sparks the public's curiosity in many ways – ethically, legally, emotionally and scientifically. Infertility, the disease that IVF overpowers, affects one million women each year. But the media rarely write in-depth articles that give readers and viewers information about the evolution of IVF and the years of trials and error that doctors and patients endured to improve the technique. Nor has the press covered the cost of IVF. That information is important to potential patients and the medical field and the history of research and medical development. This series of three magazine articles fills the information gap and also looks at the media's response to that gap.

With love to Elizabeth Lee Bickford Burnette.

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I: Introduction

Each year more than 1 million infertile women in the United States visit fertility clinics in hopes of having a healthy baby boy or girl. In 2005, the Centers for Disease Control and Prevention tentatively reported, according to latest data, that 134,242 women underwent an assisted reproductive technology, a procedure that manually combines egg and sperm to nudge life along. That year 38,910 women gave birth. The gambles of infertility treatments – which, according to the CDC, carry a 37.3 percent success rate each month, although some experts say rates are now closer to 50 percent – takes a physical, emotional, financial and moral toll on couples. Yet the outcome of having a healthy child drives the pursuit by many couples. It also makes the infertility business a $3 billion-a-year industry.

The most popular and most profitable procedure of assisted reproductive technology is in vitro fertilization – IVF for short – a procedure that extracts an egg, joins it with sperm in a Petri dish and a few days later replaces the resultant embryo back into the womb to develop. About 99 percent of couples who underwent an assisted reproductive technology in 2005 received in vitro fertilization, according to the CDC. This technology helps couples overcome many infertility problems like blocked fallopian tubes, poor sperm motility or genetic diseases that impede gestation.

Many newspaper and magazine stories about in vitro fertilization are snapshots in time, capturing scientific advances, hot moral debates or oddities. From these snapshots, many couples get information about the procedure. Yet two areas of in vitro fertilization go underreported in the media, leaving modern couples with some unanswered questions.

The first is the combined history and evolution of IVF procedures and drugs. Namely, how is the procedure different for modern couples than it was for couples 25 years ago? Scant material has been written in a comprehensive fashion explaining the nitty-gritty differences between IVF in the early 1980s versus today. The evolution of IVF and the years of trial and error that doctors and patients endured to improve the technique are important to potential patients. This insight could give couples a deeper understanding of their infertility treatment. What's more, it is important to the medical field and the history of research and medical development.

The second is why the technology cost so much. On average, IVF cost couples $10,000 to $12,000 for each cycle of treatment. Little is written about this as well.

Two British doctors, Robert Edwards and Patrick Steptoe, mastered IVF in their lab in Oldham, a town outside of London, in the late 1970s. From that venture, the world's first "test-tube baby," Louise Joy Brown, was born on July 25, 1978. She was a normal, healthy and fat baby, Anita Gates reports in a *New York Times* article.

IVF did not migrate to the United States for another three years. A renowned American couple, Drs. Howard W. Jones Jr. and Georgeanna Seegar Jones, who were both former teachers and doctors at The Johns Hopkins University's Laboratory of Reproductive Physiology, were the first to perform in vitro fertilization in the U.S. successfully. The pair moved their research to Eastern Virginia Medical School in Norfolk, Va., where they eventually mastered IVF. On Dec. 28, 1981, the first U.S. test-tube child, Elizabeth Jordan Carr, was born. At first the American public was leery of reproductive science, fearing doctors were playing God and the resultant children would be abnormal.

Yet during the last 25 years, more than 3 million IVF babies have been born worldwide, including more than 300,000 in the U.S. alone, according to wire reports and the American Society for Reproductive Medicine. The once-scary technology has become a procreation staple.

Today, in vitro fertilization has more bells and whistles than just conception. Although many procedures are possible, they are not necessarily routine or acceptable. Doctors can determine the sex of an embryo and screen for some genetic disorders through a technology called preimplantation genetic diagnosis. Doctors can perform in vitro fertilization without fertility drugs, a procedure called in vitro maturation. And what's more, doctors can remove a portion of the ovary tissue of a female cancer patient before she undergoes chemotherapy – which typically shatters fertility chances – and implant the tissue back into her uterus after overcoming cancer, thus restoring her fertility. These practices, however, are areas of research and not commonplace.

In vitro fertilization sparks hot moral debates, similar to abortion, because it deals with the moral question: When does life begin? IVF is linked to the debate about embryonic stem cell research. The infertility industry is unregulated by the federal government as rigorously as it is in other countries, such as Italy or Germany. This has put many facets of in vitro fertilization under the microscope, attracting criticism.

IVF is linked to the embryonic stem cell research debate because leftover embryos are at times donated for research. Doctors usually create more embryos than needed during in vitro fertilization to increase the chance of creating normal embryos and increase the chance of successful embryo transfers, when fertilized eggs are placed into a woman's uterus. At the end of treatment, couples have to decide what to do with the spare ones, what doctors refer

call the disposition decision. Aside from donating the embryos to science, couples freeze them for later fertility treatments, destroy them or donate them to another couple.

Embryonic stem cell research has created a sharp divide in the political arena and public opinion. The technology uses formative cells extracted from few day old embryos to generate new tissue in hopes of fighting degenerative illnesses like cancer and Alzheimer's disease, according to the National Institutes of Health. Once the cell is removed, the embryo stops growing. In a sense, it dies. That heats the debate between parties who support and oppose embryonic stem cell research.

The Bush administration does not support the technology. Embryonic stem cell research is not federally funded, except for 21 stem cell lines created before Aug. 9, 2001, when President Bush changed national policy. Many publicly funded institutions will not conduct stem cell research on federally funded equipment for fear of losing financial support. As a result an enveloping chill exists throughout public research centers in the U.S. Embryonic stem cell research remains either in private clinics or overseas, according to the National Institutes of Health.

In vitro fertilization has also been criticized for the industry's lack of regulation. The U.S. government appointed the CDC to track national success rates of assisted reproductive technology, alongside the Society for Assisted Reproductive Technology and the American Society for Reproductive Medicine. This joint venture began in 1995. Two years earlier, Congress passed the Fertility Clinic Success Rate and Certification Act of 1992 requiring the government agency to track the statistics.

Some critics refer to the U.S. as the "Wild West" of reproductive technologies because the government is not as involved in regulation as other countries, according to *The*

Washington Post's David Plotz. The U.S. government does not interfere more because of political reasons. Advocates for the left want to protect a woman's right to choose, and conservatives wish to protect a functioning, self-sustaining market, Debora L. Spar explains in her book "The Baby Business." Spar argues that a big money market exists for infertility treatment. On the other hand, reproductive industry experts say government regulation is as it should be: Clinics report to the CDC and use drugs and devices approved by the U.S. Food and Drug Administration.

Some critics, such as Spar, call the fertility business a mess. No laws stop couples from choosing the sex of their baby, a morally stigmatizing debate because opponents fear this choice may lead to designer babies where one may opt for a slender red head instead of a short brunette. In addition, few laws clarify embryo surrogacy when a woman carries a child for another. No laws allocate funding to couples attempting to pay for IVF, which costs an average of $10,000 to $12,000 per round and sometimes take more than one round for a successful pregnancy.

Other countries in Europe and the Middle East take a much firmer stance to reign in the industry. In Italy, doctors are not allowed to perform preimplantation genetic diagnosis, among other restrictions. In Germany, carrying a child for another woman – embryo surrogacy – is banned. What's more, in Israel, government officials created a pool of money to help everyday folks pay for certain fertility treatments, according to news reports.

On the other hand, other countries with more regulation also impose restrictions that do not exist in the U.S. For example, in Italy doctors are only allowed to implant three fertilized eggs into a woman, which limits the chances of a successful pregnancy for couples.

Some U.S. clinics that are part of the "Wild West" perception attract international clients. Jeffrey Steinberg told *The Washington Post* that his clinics, the Fertility Institutes of Los Angeles and Las Vegas, attract couples from China and Canada who, for $20,000, get to choose their baby's sex. A would-be father, whose full name was withheld, told the reporter: "Some people spend $50,000 to $70,000 for a BMW car and think nothing of it, but this is a life that's going to be with us forever."

Not all fertility clinics are the "Wild West;" however the mavericks have received media attention. The majority are private clinics or research clinics attached to major universities that run respectable and normal businesses.

Compounding the debate and criticism surrounding the infertility industry is that the infertility industry generates a lot of money. Various procedures create a $3 billion industry each year.

The technology began at about $5,000 to $6,000 per cycle in 1983, when the procedure was up and running, and has risen to $10,000 to $12,000 at the rate of inflation. For example, a procedure performed in 1983 that cost $5,500 would cost $11,483.13 in 2007. Yet little is written in the media explaining exactly what modern couples are paying for and why the technology's cost has not declined. Couples do have information available to them through government and national infertility association Web sites and many fertility clinics offer counseling to couples about the process, cost and emotional stress of in vitro fertilization. Yet the media have written few comprehensive articles explaining the factors that contribute to the cost.

Every year thousands of infertile women in the United States go to fertility clinics with perhaps insufficient knowledge from the media of in vitro fertilization's evolution and the economic breakdown for the procedure. This thesis aims to fill that gap.

Literature Review

Many scholars point to the popular media, women's magazines and Web sites as primary sources for people's medical decisions. Given that insight, the literature review for this thesis is broken into four main sections. The first is a review of scholarly publications on media's role in disseminating health news. The second is a review of popular newspaper and weekly magazine for articles on in vitro fertilization. The third is a look at women's health publications. The last is a review of online information about the popular assisted reproductive technology.

Scholarly Work:

Academics and professionals have written extensively about the media's impact on people's health decisions, but a small amount has been written about their effect on infertility treatment decisions, specifically. The bulk of scholarly work, typically published in the *Journal of Health Communication*, focuses on HIV/AIDS, cancer and smoking. Although these articles are not entirely germane for this thesis, the works do provide insight into the press's ability to change everyday health and medical habits – for better or for worse.

The media are the main source of health and medical advice for consumers in the U.S., stated Ann McPherson, who wrote "The problem with medical advice columns" in the *British Medical Journal* in 1999. McPherson pointed out doctors who are columnists can

often give misleading or simplistic advice. Given this power, the press has been heavily criticized for misleading the general public, especially when reporters fail to paint an accurate picture.

The press has been slammed for halting public health campaigns. For example, the worldwide press reported that six children died in India following a polio and Vitamin A double vaccine. The BBC reported that the vaccine combination may have killed the youngsters, described Dr. Scott Ratzan, an editor of the *Journal of Health Communication*, in an editorial published in 2002.

But the deaths were not caused by the vaccinations. The press got it wrong. As a result, only 47 percent of the targeted 35 million children showed up for treatment. Ratzan also pointed out that 200 million children worldwide have benefited from Vitamin A shots; the supplement can stave off malnourishment, prevent blindness and more.

Trudy Lieberman stated in her article "Bitter Pill," published in the *Columbia Journalism Review* in 2005, that the press can be persuaded by the pharmaceutical industry. Drug companies are a major source of funding for academic research. In the past when medical studies were published in major journals like *The New England Journal of Medicine, The Journal of the American Medical Association* or *The Lancet*, disclosure of financial ties was not required. Full disclosure is a standard now. Drug companies often have a stake in medical studies to get favorable results and favorable press. For example, Lieberman pointed out that the drug company Sepracor prayed upon media naiveté with its sleep aide, Lunesta. At a press conference for the drug, Sepracor Chief Financial Officer David Southwell told the media that insomnia was an unrecognized problem in society and "estimated the U.S. market for sleep aids at $3.5 billion a year and growing." He was hyping demand by creating

a problem, Lieberman noted. The conference also provided the press with two additional sources: expert Dr. Andrew Krystal and Lunesta-user Terri Bagley. Krystal was a Duke University professor with financial ties to the study. Bagley was a North Carolina business owner and a paid study participant. Testimonials from both sources appeared in the *L.A. Times, The Washington Post* and *The (Raleigh) News & Observer* without disclosing prior payment to both sources.

Although many forms of media are popular sources for health and medical information, magazines typically speak to women the most, according to Australian researcher Desley Kassulke and colleagues. Mass marketed women's magazines typically cover health topics such as lung cancer, breast cancer, nutrition, pregnancy, menopause, depression and domestic violence, Francis Bonner and Susan McKay report in their journal article, "Challenges, Determination and Triumphs: Inspirational Discourse in Women's Magazine Health Stories," published in the Australian journal *Continuum* in 2000. These articles either appear as features, informational pieces or advice columns, which are written by everyday folks or celebrities. First-hand accounts typically have similar structure: A woman recounts her diagnosis, talks about her treatment and then offers her reflections.

The phenomenon of health stories in the popular press gained in popularity in the last 40 years (Bonner & McKay p.134). The 1980s saw the biggest surge in health stories, which scholars believe rose from the public's increased interest into the personal lives of others (Bonner & McKay p. 134). In recent years, though, health information has also become more readily available on the Internet. Australian researcher Tania Lewis notes that people are more into "lifestyle" now, which includes fitness, diet and types of "risky" behaviors they choose to participate in. People in developing countries have more access to the World Wide

Web in Internet cafes and thus to information online to help make informed health decisions. As a result, online health-related groups have increased steadily since 2000, researchers from the Pew Internet & American Life Project note. Women's nongovernmental organizations in Africa are even using Web sites to help raise awareness about HIV, family planning, teen pregnancy, violence and more.

Popular Media:

In the past few years, the popular media have covered specific medical advances of in vitro fertilization, the people who made those advances, the lack of insurance coverage for fertility treatment, the risks of birth defects, fertility prolonging techniques, the debate about embryonic stem cell research, the emotional trials of IVF and oddities, like the birth of septuplets.

Newspapers such as *The New York Times, Los Angeles Times, The Wall Street Journal* and *The Washington Post* and major weekly magazines such as *U.S. News & World Report, Newsweek, BusinessWeek* and *Time* have closely followed in vitro fertilization's progression since 1978, with large advances dotting the headlines. One such step forward called intracytoplasmic sperm injection – or ICSI (pronounced ik-sē) for short – made headlines in 1992 when doctors figured out how to inject a sperm into an egg, alleviating fertility woes caused by poor swimming sperm. A technique called in vitro maturation, a spin-off technology of in vitro fertilization, made headlines in 2003 when researchers discovered a way to perform the assisted reproductive technology without fertility drugs. (In regular IVF, a woman must take $1,000 to $4,000 worth of fertility drugs to induce the body into producing a dozen or two dozen eggs for extraction.) Those eggs will be fertilized,

creating an embryo. “It’s gentler, and it’s not as expensive,” an Eastern Virginia Medical School professor Roger Gosden told *The Wall Street Journal*. Doctors also made headlines when they started implanting fewer embryos, thus reducing the number of multiple births.

The press has also covered the major players of in vitro fertilization, such as Georgeanna Seegar Jones and Patrick Steptoe. Jones received media attention when she died in 2005. Major newspapers noted her lifetime achievements – pioneering in vitro fertilization in the U.S. and discovering a pregnancy hormone that laid the foundation for today’s home pregnancy test. The press has also profiled both the first test tube babies, Brown and Carr. For the technology’s 25th anniversary, *L.A. Times* reporter Rosie Mestel describes IVF in Europe in the late 1970s versus California in 2003, although Mestel did not fully focus on the evolution of the procedure itself.

The lack of insurance coverage for fertility treatments has also made headlines. Some states – Arkansas, Connecticut and Maryland – provide some or full coverage of treatments, yet the majority of states do not. Major print news media have covered innovative money saving plans throughout the years. For example, *The Wall Street Journal* published a story on April 9, 2006, about shared-risk programs, where couples could buy up to six rounds of in vitro fertilization – again, that cost about $10,000 per cycle – for $12,000 to $20,000. If the couple did not become pregnant, they received a partial refund, some up to 70 percent. “From the couple’s perspective, you are insuring against financial catastrophe,” Dr. Joel Batzofin, the medical director of Sher Institute for Reproductive Medicine, told *The Journal*. But if the couple becomes pregnant after the first round, then the rest of the investment is lost. The press also covered biotech companies that began selling fertility drugs for a cheaper price.

As reproductive technologies gained popularity, the media also called IVF's safety into question. In 2002, *The Washington Post* ran an article that stated children born through IVF or ICSI had a 9 percent chance of developing major birth defects – such as heart deformities or large birth marks – versus children conceived the old fashion way, which had a 4.2 percent chance. For the next few years, parents were concerned whether IVF was safe. In 2003, Dr. Arthur L. Wisot wrote a letter to *The Wall Street Journal* explaining conflicting medical studies. His advice to would-be parents: "Make sure you do the simplest, safest and least expensive and invasive treatments first, before moving on to the higher-tech procedures."

The media were also fascinated with in vitro fertilization's ability to prolong fertility. It covered the phenomena of older women, over age 50, giving birth through the use of donor eggs. *The Wall Street Journal* published an article in 2002, stating that it was safe for older women to go through IVF but cautioned they would have a higher risk for developing gestational diabetes and high blood pressure. The American Society for Reproductive Medicine discouraged older women from pursuing assisted reproductive technologies "because of ethical concerns." In hopes of beating the time barrier, some women began going straight to IVF. In 2005, Leslie Bienen, who was trying for a second child and undergoing in vitro fertilization, told *Newsweek*: "Time is not your friend." She was 39 at the time.

Embryonic stem cell research has also received a plethora of media attention. Big newspapers and weekly magazines have covered the topic heavily, beginning in 2001, when President Bush banned federal funding for embryonic stem cell research at public institutions. Another wave of heavy media coverage hit in 2003, when the Society for Assisted Reproductive Technology and a West Coast think-tank released a study stating that

more than 400,000 unused embryos were frozen in the United States. Advocates for stem cell research believe these embryos could be used to create up to 275 new stem cell lines. Major newspapers followed the Stem Cell Research Enhancement Act as it was passed in both the U.S. House of Representatives and Senate. Bush vetoed the bill in July 2006, stating that research on embryonic stem cells was murder.

The emotional trials of women undergoing in vitro fertilization have also garnered attention. Melissa Cole Essig wrote a *Newsweek* editorial titled, "At 39, I want the Baby without the Blame," explaining her difficulty coping with infertility and the ignorance that some people show toward the condition.

The national press has also covered odd occurrences caused by in vitro fertilization, like a great-grandmother giving birth to her fourth child thanks to the assisted reproductive technology. "I wanted to experience birth as an adult this time," the mother Lucretia Hodges told *The Washington Post* an article published on July 13, 2001. On April 25, 2005, the *L.A. Times* published an article about a San Francisco doctor who lost his medical license after implanting the wrong embryos into a woman. The woman won $1 million in damages.

Women's Magazines:

Topics covered in the nationally circulated women's magazines *Redbook, O, The Oprah Magazine* and *Good Housekeeping* focus on the cost of having children, the dangers of fertility drugs and personal accounts of both celebrities and everyday folks. (It should be noted that few women's magazines are accessible through the University of North Carolina at Chapel Hill's library database. This section does not contain as thorough a search as the popular media section).

Redbook published an article in 2004 comparing the cost of having a child naturally versus having a child through adoption, in vitro fertilization or surrogacy. Writer Molly M. Ginty cautioned readers to think through the expense of a having a baby well in advance because the investment varies, ranging "from a mere $325 (for a natural conception) to a jaw-dropping, budget-busting $63,274 (for surrogacy)." The article offered readers tips to cut costs, such as finding partial insurance coverage if a couple was considering IVF or filing for an adoption tax credit if a couple was considering adoption and their household income did not exceed $192,390. Although this article offered couples financial advice, it did not explain to readers why IVF was expensive.

A story about the dangers of fertility drugs – such as Lupron and Pergonal – was published in *O, The Oprah Magazine* in February 2004, cautioning readers that some women developed cancer after going through IVF or taking potent medicine. "Some women – especially 'frequent fliers' who go through many cycles hoping for a baby – get more than the FDA's (recommended) limit," stated reporter Joanna Perlman. For example, *British Vogue* editor Liz Tilberis went through nine unsuccessful rounds of IVF in England in the early 1980s. Tilberis later developed ovarian cancer and questioned if the drugs caused it. She died of the disease in 1999.

Good Housekeeping has featured profiles of both celebrity and ordinary women's trials with infertility and assisted reproductive technology. Actress Alex Kingston, from the television series "ER," told the publication in 2004 that her inner fears kept her infertility treatments from being successful. In 2005, Margaret A. Peckham Clark explained to *Good Housekeeping* that she desperately wanted a child after her husband, Hal, unexpectedly died

of a heart attack at age 43. Clark had doctors remove Hal's sperm for later in vitro fertilization cycles.

Health Organization Web sites:

Four main Internet sites exist for infertility information: the InterNational Council for Infertility Information Dissemination, the Society for Assisted Reproductive Technology, the American Society for Reproductive Medicine and Resolve: The National Infertility Association. These sites feature information that offers a step-by-step description of in vitro fertilizations, the drugs involved, tips on how to cope with the emotional rollercoaster caused by treatment, insurance coverage and more. But, again, little is written detailing the evolution of IVF or the economic breakdown. Some is written about the political and social controversy about leftover embryos and stem cell research.

The InterNational Council for Infertility Information Dissemination – or INCIID, pronounced (in-sahyd) – features an article written by Dr. Jeffrey Keenan and public relations manager K.D. Oakley about the political controversy about embryonic stem cell research. Like the national press, it does a great job describing the history of bills passed through legislative bodies, and it also does a solid job laying out couples' moral dilemmas.

Issues to Explore

This thesis will explore two aspects that go underreported in the media about in vitro fertilization. The first is the evolution of the reproductive science, namely how is the technology a different experience for a woman in the United States now versus 25 years ago? The second is the economic breakdown for this assisted reproductive technology. Again, in

vitro fertilization is an expensive procedure, and scant is written detailing its cost. This information is important to potential patients, the medical community and the history of research and medical development.

Method and Limitations

The research for this thesis is a series of long-form, magazine articles on both the evolving technology and cost of in vitro fertilization. To gather data for this thesis, I conducted several in-person and telephone interviews with medical pioneers and women who have experienced the technology firsthand at various historical points between 1981 and 2007. Some of these sources had medical "firsts," such as one of the first doctors to successfully perform IVF in the United States or the first doctor to perform another assisted reproductive technology called intracytoplasmic sperm injection, a technique when a doctor injects one sperm into one egg.

I also used relevant government sources, such as the National Center for Health Statistics, the U.S. Department of Labor or the Centers for Disease Control and Prevention for data. I also used national association Web sites such as Resolve: The National Infertility Association, the InterNational Council on Infertility Information Dissemination or Medline Plus.

I used important medical studies, published in journals such as *The New England Journal of Medicine* or *The Lancet.* I reviewed medical consent forms and documentation from studies conducted in the early 1980s.

Some limitations surfaced for this thesis, such as getting interviews with specific contacts. One hurdle was getting interviews from sources at drug companies that

manufacture fertility medications. They could have added more depth to the third article, which focuses on cost. What's more, it was difficult to arrange interviews for other medical firsts, such as the first doctor to perform an ultrasound-guided transvaginal egg retrieval.

Chapter Breakdown

Again, this thesis will consist of three long-form feature articles. The first will be written in narrative structure. The second will be a long, informational piece. And the last will be written as a consumer piece. The three stories aim to fill the popular media's information gap concerning the evolution and financial considerations of in vitro fertilization. This storyline will also contain an appendix, containing a complete source list and a copy of a transcribed interview with Dr. Howard W. Jones Jr., one of the first doctors to successfully perform IVF in the United States.

II: Pioneer Doctors and Patients

For a time in the 1980s, Sarah Smith Houck drove about 30 minutes from her Virginia Beach home to a doctor's office in downtown Norfolk to have a needle stuck in her arm every four hours. At noon, 4 p.m., 8 p.m. or midnight, she met six other women, so researchers and nurses could draw blood to check the women's hormone levels and run other tests, monitoring every nuance of their reproductive cycles: These women were the pioneers of the first successful in vitro fertilization clinic in the United States.

"The only four-hour shift they let us skip was 4 o'clock in the morning," Houck, now 60, recalls. "Your veins would collapse. Your arms would be so sore. A couple girls tried the shots to stay in them all the time, but it was uncomfortable. It was rough."

Three years earlier, Drs. Robert Edwards and Patrick Steptoe were the first to successfully perform in vitro fertilization in Oldham, England. From that, Louise Joy Brown, the world's first "test-tube baby," was born on July 25, 1978. Yet the assisted reproductive technology – which manually joins egg and sperm to form an embryo outside of a woman's body – did not gain ground in the United States until two doctors moved their research from The Johns Hopkins University School of Medicine in Baltimore to Virginia. Drs. Howard W. Jones Jr. and wife Georgeanna Seegar Jones began recruiting patients to join their efforts at Eastern Virginia Medical School. They soon met Houck. She would become the Jones' first patient.

"They wanted to keep it very quiet," Houck says, because protesters were against the technology and did not want to see it in Hampton Roads, a cluster of 14 cities and counties

surrounding Norfolk. The Virginia health commissioner at the time questioned whether the lab should be in Norfolk. “The worst part was the right-to-lifers were trying to stop it,” Houck says. “We had to go to this big meeting and the right-to-lifers were screaming, ‘Incest! Incest!’ It was horrible.”

After holding the public hearing, the Joneses received a green light to continue their research. Houck showed up in pajamas to Norfolk General Hospital for her first procedure, but wasn’t sure what to tell the check-in nurse, who asked: ‘OK, what are you here for?’

“And I said um, ‘I guess you need to ask Dr. Jones’,” Houck recalls. “It was all hush, hush, hush, hush.” Houck was a health and physical education teacher for the Virginia Beach public school system. Her now ex-husband Bob Smith was also part of the school system. “(The procedure) just wore you out. And then trying to keep it a secret and still teach school.”

The doctors were trying to discover the intricacies of what makes in vitro fertilization work. To do so, doctors at Eastern Virginia Medical School conducted a series of studies, many of which Houck participated in.

“It was one big waiting period for all six of us to go through this thing,” Houck says about the first study. “The Joneses would meet every afternoon with all the doctors, and they’d compare this patient and that patient.”

Theory Years

In the beginning, it was trial-and-error to mimic natural reproduction at Eastern Virginia Medical School, as it was at other institutions. Doctors were unsure which nuances

were important in a woman's body and should be recreated in the lab and which ones didn't matter.

"In 1980, there was a suspicion that you had to work in the dark because it was said the sperm and the egg had never seen light," Dr. Howard W. Jones, Jr., now 96, explains "And, therefore when we first started we used infrared lights in the laboratory." Using infrared lights turned out to be unnecessary.

During IVF, doctors extract a woman's egg and join it with sperm in a Petri dish to form an embryo – which usually takes three to five days – and then place that embryo back into the woman's womb for it to implant and turn into a viable pregnancy. Because fertilization naturally occurs inside a female, doctors were unsure what pH level the Petri dish medium should be to match a woman's biology.

"We started out with a pH of 7.2; 7.4 turned out to be the better pH," continues Howard Jones, a professor emeritus at both The Johns Hopkins University School of Medicine and Eastern Virginia Medical School.

What's more, doctors were unsure how hot or cold the lab should be and if that detail was significant, because embryos naturally form in the body at 98.6 degrees Fahrenheit. "We didn't know what the effective (lab) temperature was, for instance," says Howard Jones, who consults for the Jones Institute for Reproductive Medicine, a clinic named in honor of him and his wife in Norfolk. "Edwards and Steptoe worked in England where the laboratories are traditionally colder than they were here." English labs were kept around 60 degrees Fahrenheit; U.S. labs around 70. "It turned out you can risk a little cooling but you can't overheat," he continues. "And I could go on as to the various problems that had to be solved."

All of these subtle nuances – theory by theory – had to be worked out. And as the doctors mimicked in utero conditions in their labs, they also tried to extract eggs and implant embryos during a woman's natural hormonal cycle. When Edwards and Steptoe successfully performed IVF in England, they did so by retrieving an egg before a woman ovulated, rather than by controlling her ovulation with medication, a common practice today. Doctors repeatedly tried regulating a woman's cycle with the drug Perganol, but failed. Doctors retrieved the egg through a small incision in a woman's lower abdomen, guided by a flexible tube that is a visual instrument called a laparoscope, according to MedLine Plus. This technique is called a laparoscopy. Next the eggs were joined that with sperm in a Petri dish to create an embryo. "This meant you had to estimate when a patient was going to ovulate," Howard Jones explains.

Before moving on to their first IVF attempt, researchers at Eastern Virginia Medical School tracked their first patients, like Houck, for two natural menstrual cycles to discover "each particular patient's quirks," Howard Jones says. To remove eggs before ovulation, Houck and other patients had daily blood tests, urine tests, and cervical and vaginal exams. The women also kept basal body temperature charts to help doctors track monthly hormone spikes and drops. Researchers wanted to pin down a hormone spike called an LH-surge that predicts ovulation. At the time, doctors did not know how long that window of time lasted between the surge and ovulation. Doctors today know that it is about one to two days, according to the American Association for Clinical Chemistry.

Every detailed counted, they learned. Once doctors knew each patient's idiosyncrasies and the time between hormone spikes and ovulation, it was time for the real cycle. Doctors moved quickly when ovulation was close and time for the egg retrieval, Jones

says. “We often did the laparoscopies in the middle of the night in order to accommodate this.” Even outside factors did not stop them.

“March of 1980, I guess it was,” Howard Jones recalls, “We had a very big snow storm – there was three feet of snow, and we had a patient that was scheduled for laparoscopy at 1 a.m. I left home at 7 o’clock that night with the snow and didn’t get to the hospital until 1 o’clock because of the difficulty. And it was 5 a.m. before everybody that was necessary – including the patient – was able to get to the hospital. And when we laparoscoped her we were not surprised but nevertheless disappointed to see the stoma in the ovary because she obviously ovulated,” Howard Jones continues. “We had missed it.”

In the first year at Eastern Virginia Medical School, the doctors performed more than 40 laparoscopies, fertilized and transferred 17 eggs, but saw no pregnancies, says Howard Jones. “We were disappointed, of course, in the inadequacy of the cycle.”

The problem was that doctors were relying on a woman’s natural hormonal shifts, which can vary month to month.

“It was a rollercoaster,” Houck says, who did not get pregnant through her first seven cycles of IVF. “Am I gonna ovulate? Are they gonna get an egg then? Will they put it back in? Will it fertilize? You’d have to wait about 10 days to find out if it worked.”

Bound by Adversity

In the beginning, to insure that those who became pregnant were pregnant through IVF and not by intercourse, the Joneses selected women with tough medical histories. Most had damaged or removed fallopian tubes, as it would be impossible for these women to become pregnant on their own. Houck’s fallopian tubes did not work properly. Other women

had experienced ectopic pregnancies – when a fertilized egg implants outside the uterus – before signing up for the studies. Ectopic pregnancies usually cannot be carried to term; it may risk a woman's life. "We didn't do normal infertile couples," Howard Jones explains.

"What we have here is the hard core – the couples who really, really want children," Georgeanna Jones told *The Virginian-Pilot* on Jan. 6, 1980. "But Jones is not one to give false hope and even she acknowledged that there are few statistics on the success or failure rate of in-vitro fertilization," the story continued. Georgeanna Jones died in 2005 as a professor emeritus at both The Johns Hopkins University School of Medicine and Eastern Virginia Medical School.

During the early years of trial and error, patients befriended one another in the waiting room, either when they were waiting to have blood drawn or waiting for pelvic ultrasounds, a technique used to evaluate the ovaries and measure the thickness of the uterine lining. Camaraderie grew.

"They would sit in there and drink water or Coca-Cola, or whatever it was – fluid – and then when their bladder was full they'd raise their hands and try to come in to be ultrasounded," Howard Jones recalls. "And that would be a daily occurrence; that we would do everyday, so that the patients got to know each other and often formed friendships that lasted for life."

"They kept saying, 'Drink water! Drink water!'" Houck says. "I was so sick. I was like up to my ears, drowning in water." A full bladder allowed doctors to see more clearly during a woman's pelvic ultrasound.

"We just all had to do it together," Houck says. "And a lot of (IVF) you had to keep your sense of humor … or just forget it."

"There were a lot of jokes when guys had to go get their sperm, 'Read a magazine!' You just had to roll your eyes and laugh," she continues.

Houck became friends with one woman she went through several cycles with. They would send each other Christmas cards and updates. The Joneses took the time to get to know the patients, too. They would invite the couples to their house for dinner and hosted reunions many years later.

Some couples Houck never heard from again. She kept a journal, detailing her experience. "One of the girls – it was so sad – when they went in to retrieve her egg, they slit her bladder. She got a horrible infection," Houck says. "I pray for (the couple)," she read from her diary, "that they pull through this."

"I felt so lucky that my own procedure didn't…," Houck trails off as she reads from her diary aloud, "We have to look ahead and hold on to each other," Houck continues reading: "It could have happened to any of us."

As pioneers, the women faced risks and dealt with uncertainty. The Joneses helped each woman through it the best they could. Throughout it all, the patients were under the microscope as visiting doctors and the media closely followed the Jones's progress. The experiences also bonded the pioneers.

During Houck's embryo transfer other doctors looked on. "That was tough on us because they always had all of these visiting doctors from other countries and everything," Houck says. "It was really embarrassing…You were just wide open to the world, and so I never liked that part. I was always very tense, and Dr. Georgeanna would always come over and cover me up."

The first patients also shared a sense of "adventuresomeness," Howard Jones says "There was a frontier experience because nobody really knew how it was going to be."

Medical patients faced with low odds, such as some cancer patients, are often bound by adversity, explains Dr. David Walmer, chief of reproductive endocrinology at Duke Fertility Center. "So part of it may have been that the pregnancy rates were very low; what they were going through was very intense."

The media heightened the intensity for Houck. "When the news people found out what was going on, they started banging at our door and lying to us," she recalls. They expected her to be the first woman to carry a "test-tube baby." "The National Enquirer called the school system and left a message for me to call them," Houck read from her journal. Other publications called, too: *The Globe*; *The Detroit News*. NBC network anchorman Bob Hager delivered a national newscast from Houck's den. "Everyday the Joneses would call and say, 'It's OK to talk to this (media outlet) if you want to, but this one, we said absolutely no.'"

Everyone was waiting for a successful birth.

When the Drugs Took-Off

In January 1981, Dr. Georgeanna Jones had an idea: Bring Pergonal back and regulate the women's hormone cycle, eliminating guesswork. IVF success rates took off at Eastern Virginia Medical School. Pergonal, a drug that induces a woman to ovulate, was typically used in patients who could not ovulate on their own, Howard Jones explains.

"(Georgeanna) had experience with it in anovulatory patients and had no problems with pregnancies and so forth and thought it could be used with ovulatory patients, which

was contrary to what Edwards had thought, because he had tried it and failed and said it shouldn't be used."

In early 1981, the Joneses started the Pergonal, using a low dosage. Using drugs to make a woman produce many eggs is called ovarian hyperstimulation, a technique widely used with IVF today. Judy Carr got pregnant and that first year, I think we had five pregnancies," Jones says.

Dr. Mason Andrews delivered Judy Carr's daughter, Elizabeth Jordan Carr, on Dec. 28, 1981. The United States had its first IVF baby.

Houck would go through seven rounds of IVF between 1980 and 1985 that did not work. She became part of doctors' and researchers' efforts to refine and improve IVF. "They would just cheer you on. Come on in. Don't give up; don't give up. It's gonna take us awhile," Houck recalls. "They would always call me up when they wanted to try something new. 'Sarah, could you come in? Let us try this – different drug or different procedure."

Houck always did. She signed up many studies, such as the "Vital Initiation of Pregnancy Program" and the "Regulation of Ovulation by 'pure' FSH versus FSH:LH Combination Therapy (Pergonal), Clomid, LH-RH, or any other Ovulatory Substance which may become available."

"We had a lot of guts and fortitude," she says. "I surprised myself a lot of times that I had the guts to hang in there. I just wanted it."

Using fertility drugs, such as Pergonal and Clomid, "improved the efficiency dramatically," says Dr. William Keye Jr., who was the president of the American Society for Reproductive Medicine from 2001 to 2002.

In the mid-1980s, researchers changed the way they retrieved eggs. Instead of doing a laparoscopy and entering a woman through the abdominal area, doctors began using an ultrasound-directed needle to remove the eggs transvaginally. This allowed IVF to become an outpatient procedure and move out of the operating room into private clinics. As a result, private fertility clinics began to spring up around the United States. “That was the beginning of a big trend for IVF,” continues Keye, the director of the division of reproductive endocrinology and infertility at the William Beaumont Hospital in Royal Oak, Mich.

At age 38, Houck went in for her final try. After seven let downs, she and her husband decided it was worth one more shot. She called the Joneses to see if she was too old to undergo treatment. They told her to begin the next day. On Aug. 28, 1985, after 20 hours of labor and a cesarean section, she gave birth to her twins, Ashley and Heather. “They said when Heather came out, she said, ‘Hiii!’ The doctor said it was the most emotional birth she had ever seen in her life.”

The dramatic breakthroughs that enabled Houck to become pregnant less than four years after Judy Carr showed the speed of refinements in IVF. And theses improved techniques were the beginning of even more advances that would boost the IVF success rate to 50 percent in the next two decades.

III: Growth Years and Refinement

Heather Cimuchowski was infertile for almost five years before becoming pregnant with twins in November 2006. She tried different drugs and assisted reproductive technology before she and her husband, Jon, who live in Seattle, decided to try in vitro fertilization.

In vitro fertilization, or IVF for short, has a lot to offer modern couples, like the Cimuchowski's. Success rates are high. On average, a healthy woman aged 35 or younger has a 50 percent chance of getting pregnant with each IVF cycle, according to some clinics. Plus, the technology has proven itself time and again. More than 3 million children worldwide have been born from in vitro fertilization, according to wire reports. And more than 300,000 have been born from the streamlined, outpatient procedure in the United States, according to the American Society for Reproductive Medicine.

"I only had to do it one time," says Cimuchowski, 33, a legal researcher. She had no problems while she underwent IVF, a procedure that manually joins both egg and sperm outside of a woman to form an embryo, which is then placed back into a woman's womb to become a possible fetus.

The couple tried to get pregnant for a year and a half before Cimuchowski's general practitioner referred her to a fertility specialist. At first, she did not want to go because she was worried about cost. One round of in vitro fertilization costs $10,000 to $12,000 on average. Plus, she was afraid of needles.

Cimuchoswki took the oral fertility drug, Clomid, to enhance her egg production, but she did not become pregnant. She also tried three intrauterine inseminations, when sperm is

manually placed into a woman's uterus. But that technique didn't work either because Cimuchowski has a blocked fallopian tube. Women who have blocked or damaged fallopian tubes are typically not good candidates for artificial insemination, according to the Mayo Clinic's Web site, because a fertilized egg cannot make it to the uterus successfully.

"(IVF) was really the only way we were going to get pregnant," she explains.

Cimuchowski learned about in vitro fertilization through a support group, offered through Resolve, a national infertility association, which she joined to cope with the emotional stress of infertility. Infertility carries the same rates of depression and anxiety as cancer and AIDS, writes Alice Domar in the online article "The Relationship between Stress and Infertility." Domar is an assistant clinical professor of obstetrics, gynecology and reproductive biology at Harvard University.

Other support group members talked about their positive experience undergoing in vitro fertilization, and Cimuchowski decided it didn't sound too bad. She'd give it a shot.

She researched fertility clinics in her area and decided on Seattle Reproductive Medicine because it had a shared-risk program, which is a pooled investment among several couples. This plan gave her three IVF cycles with fresh embryos and three with frozen embryos for $20,000. If those six cycles failed, the couple would receive 70 percent of their investment back.

Cimuchowski knew she had a good chance of getting pregnant the first try, but she liked the calmness she felt knowing she had five more attempts. "I don't regret doing (the shared-risk plan) even though I got pregnant the first time," she says.

This simple procedure for Cimuchowski, as it has for thousands of couples who go through in vitro fertilization every year. But that has not always been the case for couples

undergoing in vitro fertilization in the past 25 years, especially in the early years when IVF success rates were between 5 percent to 8 percent for each attempt. The industry has made leaps and bounds. Drs. Howard W. Jones Jr. and his wife Georgeanna Seegar Jones performed the first successful IVF procedure in humans in the U.S. in Norfolk, Va., in 1981. Along the way, it has realized many notable milestones.

Growth Years

By the end of the 1980s, infertility doctors in the United States had success rates between 10 and 15 percent. Doctors started using synthetic hormones – such as the drugs Clomid and Pergonal – to enhance and control ovulation. Physicians turned in vitro fertilization into an outpatient procedure, by retrieving eggs transvaginally rather than through an incision in the abdomen. Doctors were also able to freeze eggs for use in later IVF cycles, in case couples decided to have more children in the future. The medical procedure was beginning to come into its own thriving industry.

In the 1990s, in vitro fertilization expanded and matured as a procedure. They grappled with IVF working too well and the rise of multiple gestations – twins, triplets and up to septuplets. And researchers began refining their techniques from how to grow embryos to maintaining the right laboratory environment. Doctors realized their biggest advancement to date.

Intracytoplasmic sperm injection, or ICSI (pronounced ik-sē) for short, is in vitro fertilization's most notable milestone to date, says Dr. William Keye Jr., president of the American Society for Reproductive Medicine in 2001 to 2002. "That has had the greatest impact of anything we've ever done."

During traditional in vitro fertilization, doctors and researchers place both eggs and sperm into a Petri dish and allow sperm to naturally swim and enter the oocytes, another term for eggs. If the sperm had poor motility and could not swim to and into the eggs, fertilization did not occur.

ICSI, which uses a needle to inject a single sperm into one egg to achieve fertilization, is the best solution to treat male infertility. Clinics worldwide were trying to master a procedure similar to ICSI in the 1990s, but were unsuccessful because they had not developed the right needle. No one had gotten the procedure right.

Dr. Gianpiero D. Palermo, an Italian scientist, became a visiting professor at the University of Brussels in Belgium in 1988. He was working at a large fertility clinic where doctors performed 1,500 cycles of in vitro fertilization year, a high number for that time. Forty percent of patients had male factor infertility, such as sperm that are poor swimmers. The clinic was aggressively pursuing an answer to this problem, Palermo explains. Clinics worldwide were trying to master a procedure similar to ICSI, but were unsuccessful.

“At first people didn’t understand that you could go into the egg without breaking it,” explains Palermo, now the director of assisted fertilization and andrology at The Center for Reproductive Medicine and Infertility in New York and associate professor at the New York Presbyterian Hospital–Weill Medical College at Cornell University.

“The problems were technical and not physiologic barriers,” says Dr. David Walmer, chief of reproductive endocrinology at Duke Fertility Center. The challenge was creating a needle that was small enough to enter but not harm the egg.

So Palermo made his own needle. It was a microneedle, one-fiftieth the size of a pinhead: It worked.

Palermo and researchers achieved their first successful pregnancy through ICSI in October 1990 but waited until July 1992 to publish their results in both *The Lancet* and *The New England Journal of Medicine*. "We waited for the delivery of the child," Palermo says, before publishing the findings – just to be safe. By the time the study was published, four children had been born from embryos fertilized by ICSI, according to the studies.

Precision was also increasingly important with ICSI. To inject one sperm into one egg, doctors had to pay close attention to other steps, Palermo says. Doctors had to remove the outside cover of the egg, called the cumulus. Doctors had to wash the egg in a special solution to remove impurities. What's more, doctors had to carefully select each sperm – some sperm are overly aggressive or carry toxins – and pay close attention to the medium and incubator, Palermo explains.

"It was an IVF of its own," Palermo says. "It was an entirely different world." Also, by removing the outside of the egg – the cumulus – doctors could see the oocytes more clearly and determine the egg's level of maturity. Doctors would perform other procedures in the future using this needle and new vantage of the human egg, Palermo adds.

The use of ICSI quickly spread. "Once it happened, the technology transfer was incredibly rapid," Walmer says. "People everywhere were doing it."

"The people doing IVF are very skilled technically," he continues. "They just need to have someone make that breakthrough."

By 1995, ICSI was "pretty commonplace" throughout fertility clinics, says Keye, the director of the division of reproductive endocrinology and infertility at William Beaumont Hospital in Royal Oaks, Mich. "It probably doubled the potential number of candidates for IVF," he says, by treating male factor infertility.

During the 1990s, in vitro fertilization almost became too good. In the 1980s, doctors would implant sometimes up to six embryos into a woman's uterus because multiple pregnancies were rare. We were "so lucky to get pregnant," Keye explains. Doctors began to realize they were going to have to face the issue of multiple pregnancies.

In response, the American Society for Reproductive Medicine began publishing in the 1990s guidelines for the number of embryos doctors should implant. Limiting the number of fertilized eggs implanted in a woman's womb would decrease her chances of multiple births.

Doctors also began to grow embryos in the lab longer. In the past, embryos were grown for about three days. However in the 1990s, doctors discovered Petri dish cultures with better nutrients, incubators and lab conditions that would keep the embryos alive longer outside of the body. This development allowed scientists to select more carefully the embryo to implant. It also opened the door for a procedure called preimplantation genetic diagnosis, or PGD for short.

This technology allowed doctors to extract a single cell from an embryo only a few days old to test it for genetic defects, such as a hereditary disorder. Researchers hoped pre-implantation genetic diagnosis could help doctors achieve and maintain pregnancies in high-risk women, such as women age 38 and older or women with reoccurring miscarriages.

"The aim of PGD is to guarantee that any pregnancy initiated is healthy," Dr. Santiago Munné wrote in a journal article published in the *Current Opinion in Obstetrics and Gynecology* in June 2002, "and that there will be no need to contemplate termination of an affected fetus."

In the 1990s, doctors also started paying more attention to the air quality in their laboratories, although formal studies had not been published on this topic. Researchers began

to positively pressurize their laboratory air to "push out" impurities, which is "thought to be very important by embryologists," Keye says.

Refinement

In 2002, 1.2 million women out of 62 million women of reproductive age had an "infertility related medical appointment" in the U.S., according to the Centers for Disease Control and Prevention. That number is about 2 percent of the childbearing population.

In vitro fertilization had grown to a multi-billion dollar industry. Most of the ground work for treatment had been laid, and since then "we've mostly refined the techniques," explains Keye about the industry since 2000. The last seven years have also been a time for new technology and upping the standards of both embryo transfers and lab quality.

Specifically, doctors with access to molecular biology labs can use preimplantation genetic diagnosis to single out single gene defects that carry diseases such as muscular dystrophy. Although this technique is promising, it is not yet widely used, says Walmer, and remains a hot research area, although controversial.

"The dilemma is that early embryos are often mosaics," Walmer says. "You could have one cell that goes awry and the rest of them could be OK, or different proportions of that. So you don't know for sure. When you're looking at gross abnormalities that are not very specific to a family that cell may or may not reflect the rest of the embryo, and so we're not sure yet whether or not you can make an accurate diagnosis of some of these things you can find based on one cell."

Researchers also tried another technique called in vitro maturation, a spin off of in vitro fertilization. During in vitro maturation, doctors retrieve an immature egg that has not

been stimulated by medication, a common practice during traditional in vitro fertilization. Its success rates remain low, and like preimplantation genetic diagnosis, in vitro maturation remains an area for research.

What's more, the American Society for Reproductive Medicine also set forth stricter embryo transfer guidelines, decreasing the number of embryos that can be implanted at one time from three in 2003 to implanting two embryos in 2005. Doctors hope this number will drop to one someday, Keye points out.

Also, fertility clinics began to pay even more attention to air and environmental quality, a move that had begun in the 1990s, Walmer says. Some started building custom facilities. The new facilities are built from the ground up with a goal to keep outside chemicals away – a step up from using older labs that are positively pressurized to push out impurities. This is another level to trying to create a space that is more like the cervix, uterus and fallopian tubes, Walmer adds. Duke Fertility Center moved into its new facility in Durham, N.C., in 2006.

Modern Experience

By the time Cimuchowski got to in vitro fertilization in 2006, the procedure was fine-tuned. She experienced what modern couples experience. "It was a pretty simple procedure for me," she explains.

She went in for pre-testing – which included a Pap smear exam and AIDS testing. She then spoke with doctors and counselors at her fertility clinic about options and cost and then started the process.

Today women start an in vitro fertilization cycle by taking birth control pills for one month to regulate their hormonal cycle. Next, some women take a drug called Lupron to flat-line all of the hormones in their body, similar to what a woman experiences during menopause when hormone levels decrease. This allows doctors to work with a blank slate. Next, women start self-administering injectable drugs for two weeks to induce ovulation and to help the eggs mature. The egg retrieval follows. Then eggs are fertilized and allowed to mature in a Petri dish for three to five days. Last is the embryo transfer.

The only snag Cimuchowski had to overcome was her fear of needles.

"I got through it because I knew I had to," she says. She and her husband Jon administered her fertility drugs.

On Oct. 23, 2006, she went in for her transvaginal egg retrieval, an outpatient procedure that took about half of the day, she recalls. "They knocked me out for that," by giving her general anesthesia. The doctors retrieved 10 eggs – she had responded well to her fertility drugs – and incubated those eggs along with her husband's sperm for five days. Cimuchowski said she was "really excited" because she had heard five-day transfers had higher success rates. Two embryos made it to the level of blastocytes, which are small clusters of cells, slightly more developed than embryos, yet only the size of a small dot.

On Oct. 28, 2006, she went in for her embryo transfer. In the clinic, on a TV screen she could watch the doctors work, "sucking up the tiny little embryos and transferring them," she says. The doctors implanted two fertilized eggs.

"They gave us a picture of the two embryos as they were transferring, which was really cool," she says. After the embryo transfer, she stayed still for about 30 minutes. "Then they just let us go," Cimuchowski says.

On Nov. 7, 2006, she found out she was pregnant. “It was very, very positive,” she says because her hormone levels were high. “So I wasn’t really surprised…when I found out I was having twins.” When she was eight weeks along, Seattle Reproductive Medicine released her to an OB/GYN.

While going to the clinic, Cimuchowski got to know the doctors and nurses but didn’t build camaraderie in the waiting room, as did the pioneering women did in the early days of in vitro fertilization research at Eastern Virginia Medical School in Norfolk, Va. Many of those women who shared days of blood tests and ultrasounds became friends.

Instead, Cimuchowski found her friends through infertility support groups and through Internet blogs during the years before she underwent IVF as she coped with infertility.

“There are a lot of patients with infertility that seek each other out for emotional support and support groups,” Walmer says. “And maybe that’s different than being in a waiting room.”

Cimuchowski read the infertility blogs “And I Wasted All That Birth Control” and “So Close.” The latter was written by Tertia, a 38-year-old South African woman who went through nine cycles of in vitro fertilization, according to her blog.

“I just thought it’d be a good place to release emotions,” Cimuchowski says. “I just decided to do the same.” Cimuchowski started her blog, “Desperately Seeking Baby,” that she has updated along her journey. “It really helped me to learn and see what other people were going through.”

“The blogs definitely gave me a sense of community,” she explains.

Cimuchowski's twins, a boy and a girl, were due July 16. Her OB/GYN believed she would deliver early because Cimuchowski's cervix was thinning and because she was having frequent contractions. Cimuchowski was on bed rest in Seattle, blogging her experience – her very modern experience – until June 12, the day her newborns, Benjamin and Ella, came early.

IV: The Bottom Line

Throughout the last six years, Mary, whose name has been changed for this article, has spent $30,000 out-of-pocket on infertility treatments in hopes of having baby. Mary and her husband have also maxed out each of their company's medical spending plans for two straight years, finagled with her insurance company and taken out an equity line on their home to pay for her infertility treatments.

"We decided quite a long time ago that we were gonna exhaust all of our possibilities to have a child on our own before we started exploring adoption," says Mary, a 36-year-old East Coast banker who lives in Southeastern Virginia.

Since 2001, Mary has taken fertility drugs, undergone seven intrauterine inseminations – when sperm is manually placed into a woman's uterus – and one round of in vitro fertilization, or IVF for short. In IVF an egg is fertilized outside of a woman's body then transferred back into the uterus to implant and possibly develop into a fetus.

"The decision to go through IVF was huge for us because of the expense," Mary explains. On average, in vitro fertilization costs $10,000 to $12,000 each round. "Not only are you going through this huge, emotional roller coaster of do I want a baby, or do we want to adopt? Obviously, none of it is guaranteed."

Mary underwent her first round of in vitro fertilization in April 2007, but it failed. She will do her second round of IVF this July at the Jones Institute for Reproductive Medicine in Norfolk, Va.

At first she was leery of working with the clinic. “I didn’t think that I could afford the Jones Institute,” Mary says. The Jones Institute for Reproductive Medicine was the first clinic to perform IVF successfully in the United States in 1981.

In her mind, Mary continues, royal families from Jordan or wherever went to the Jones Institute for treatment. “But little old me, we couldn’t afford it,” she says.

Once she found out how much it cost, Mary and her husband realized they could afford the institute. “We’re both doing well,” Mary says. Her husband also works in finance. “(But) the average person – I don’t know how they afford this.”

Mary’ first round of IVF cost slightly more than average. Her total came to around $13,620 for her treatment, which included drugs, laboratory costs, egg retrieval, embryo transfer, anesthesiologist fees, freezing the embryos and more.

“It’s a lot of money. I’m not gonna say it’s not. But I mean, if we go out and buy a car today, it’s going to be a $40,000 car. In the scheme of things, what’s really important in life?”

The cost of in vitro fertilization has risen from $5,000 to $6,000 in 1983 – two years after it was first successfully performed in the United States – to today’s average of $10,000 to $12,000. The cost has risen at basically the rate of inflation, according to the U.S. Department of Labor. A procedure that cost $5,500 in 1983 would cost $11,483.13 in 2007. The cost of new technology typically is expensive, and then the cost comes down later. But that hasn’t been the case with IVF.

The price plateau has many facets to it. The cost of health care in general has risen in the past 25 years, making it harder for the cost of the procedure to decline. The cost of fertility drugs remains a big market for pharmaceutical companies. And clinics are operating

with more quality control, which is expensive. All of these factors combined have kept the price of IVF holding steady at a high cost. Yet some doctors say modern couples undergoing IVF may be getting more services for their money than 25 years ago. In that sense, the actual cost may be declining.

Start-Up Cost

Sarah Smith Houck was one of the first patients to undergo in vitro fertilization at the Jones Institute for Reproductive Medicine between 1980 and 1985, but she was not the first woman to have a successful in vitro pregnancy. Judy Carr gave birth to the country's first "test-tube baby," Elizabeth Jordan Carr, on Dec. 28, 1981.

Houck underwent many pioneering experiments with Drs. Howard W. Jones Jr. and Georgeanna Seegar Jones along their journey to become the first doctors in the United States to make in vitro fertilization work in humans.

Houck went through seven rounds of in vitro fertilization before she gave birth to her twin girls, Ashley and Heather, on Aug. 28, 1985. In the beginning the cost of her treatments were mostly covered by the Jones's research funding. Later that changed, and Houck's out-of-pocket costs increased.

According to Houck's bill for the Vital Initiation of Pregnancy Program in 1981, she received two rounds of IVF for $1,000; the package would have otherwise cost $3,920.

This cost included $2,160 for the egg retrieval and embryo transfer, $1,000 in hospital charges, $300 for anesthesiologist fees, $360 for laboratory charges and $100 for administration fees. The charge also included the cost of the fertility drug Pergonal, used to stimulate egg production.

By 1983, the cost of Houck's in vitro fertilization treatment had reached $5,000 to $6,000. Dr. William Keye Jr., former president of the American Society for Reproductive Medicine, agreed that this price range is more accurate than $4,000, which has been published in the past as the early rate for the procedure.

Houck says the hospital cost caused the price to increase during 1981 to 1983, not fertility medication or other fees. By the time she became pregnant in 1985, the cost went to $8,000 per round of IVF, says Houck, who taught physical education for the Virginia Beach public school system. "Teachers didn't make that much money," she continues. "Every dime we had was going into that."

Houck was able so save some money on her treatment, in comparison to other pioneering patients. Most of the patients who underwent IVF at the Jones Institute for Reproductive Medicine in the early years were from out of town, says Houck, who lives in Virginia Beach, about 30 minutes away from downtown Norfolk where IVF procedures were performed.

"We were local. We didn't have to spend money on hotels," Houck says. She wouldn't have been able to afford IVF otherwise.

Holding Steady with Inflation

Since the 1980s when Houck underwent in vitro fertilization, the price of medical care in general has increased tremendously. Inflation accounts for some of IVF's leveled off cost.

The Consumer Price Index – which measures the price of a basket of goods by eight major industries such as housing, food and beverages, apparel, transportation – gauges cost

fluctuations and is used by economists to measure inflation, according to the U.S. Department of Labor. In January of 1982-1984, the Consumer Price Index for all items was 100. By January 2005-2007, the index for all items was about 200. Groceries, gasoline, milk and medical care are all two times more pricy now than about 20 years ago.

This increase was more predominant in medical care. The Bureau of Labor Statistics, which releases the Consumer Price Index monthly, splits the medical care industry into two sections: Medical care commodities that include drugs and medical supplies and medical care services that include professional services, hospital fees and health insurance.

The index for medical care commodities, which include fertility drugs, rose 186 percent from 100 in 1982-1984 to 286 in 2006. This is 43 percent higher than the price increase for all items.

Medical care services, which include the costs of receiving treatment at a fertility clinic, rose 251 percent from 100 in 1982-1984 to 351 in 2006. This is 76 percent higher than the price increase for all consumer items.

The rise in both medical care commodities and medical care services is higher than increases in the price of housing, transportation, and food and beverage. Higher hospital costs, expensive nursing home and home health care, pricey medications and physician fees are driving increases in the medical care industry, according to the article "Health Care & The 2004 Elections," published by The Henry J. Kaiser Family Foundation, a California-based nonprofit that specializes in health policy and also serves as a health information clearinghouse.

IVF does not reflect increases that the general medical field has experienced, although it was lumped together with other procedures in medical indexes. In vitro fertilization's cost is less inflated than other medical procedures.

"We don't base our cost on what other health things are," says Dr. David Walmer, chief of reproductive endocrinology at Duke Fertility Center. IVF clinics do not set their prices based on the cost of general health care.

Expensive Fertility Meds

Fertility drugs also contribute to the high cost of in vitro fertilization, even though they are not the main driver.

Today, more fertility drugs are on the market than in the 1980s. Some modern drugs are more technically advanced than some older medications.

In the 1980s, the major fertility drug for in vitro fertilization was Pergonal. Dr. Georgeanna Jones resurrected this drug in 1981 and made in vitro fertilization successful.

The first doctors to perform IVF in the world, Drs. Robert Edwards and Patrick Steptoe, relied on a woman's natural ovulation cycle. For each attempt of in vitro fertilization, doctors tracked a woman's hormone fluctuation and retrieved an egg right before she ovulated.

"This meant you had to estimate when a patient was going to ovulate," says Dr. Howard Jones Jr., 96, who still consults for the Jones Institute for Reproductive Medicine, "And that wasn't easy."

This guessing game changed with Pergonal, an injectable hormone that makes a woman's body produce more eggs. The once Italian-based drug company Serono first

manufactured Pergonal, which is derived from the urine of post-menopausal women, in 1948, according to the Web site of Merck Serono S.A., the company's new name. This source made the drug "natural," according to the Jones Institute for Reproductive Medicine's Web site. Modern versions of Pergonal aren't derived from urine but rather from recombinant proteins, synthesized in a lab.

Now more drugs are used in IVF, which use to dominate the market, faces competition for market share from TAP Pharmaceutical Products Inc., Organon International, Solvay Pharmaceuticals Inc. and more. The fertility drug market is a $3 billion-a-year industry.

"If somehow the cost of drugs came down, we'd all be better off," says Howard Jones. "But I don't see that happening in the near future. The drug companies have a bottom line, just like everybody else."

On average, doctors at the Jones Institute for Reproductive Medicine tell modern couples to set aside $3,000 for fertility drugs. Sometimes the medication can cost more or less, depending on the woman's prognosis and insurance coverage, patient Mary says.

For Mary, her drugs cost only $400 because they were covered by her insurance carrier. "I mean, I couldn't get my credit card out quick enough," Mary says. "I was lucky when it came to medicine."

During a typical round of IVF, a woman will take birth control pills to first regulate her hormones. Then she will take a drug called Lupron, manufactured by TAP Pharmaceutical Products Inc., to flat-line those hormones – similar to menopause in older women – eliminating spikes.

Next she will take an injectable drug to stimulate egg production, such as Gonal-F, which competes with Organon Inc.'s drug Follistim for market share. The cost of injectable drugs varies on dosage. For example, Mary took a daily dose of 300 IU, which cost her $200 a day for ten days straight, or $2,000.

Women will then take a drug to trigger ovulation, such as Ovidrel, which is made by Merck Serono S.A., Novarel, which is made by Ferring Pharmaceuticals, or Pregnyl, which is made by Organon. Next IVF patients will take Progesterone, which helps thicken the uterine lining, creating a plush environment for an embryo to implant and develop.

Although fertility drugs are expensive, they only account for one-fourth to one-third of the overall cost of treatment. "Medications are not the major cost," explains Keye, the director of the division of reproductive endocrinology and infertility at William Beaumont Hospital in Royal Oak, Mich.

Crux of Today's Cost

The crux of in vitro fertilization's expense for modern couples is lab costs; IVF is mostly performed as an outpatient procedure. Several factors play into this price – from keeping up with government regulation, the price of instruments, specific procedures like ultrasounds or intracytoplasmic sperm injection – when a single sperm is injected directly into an egg – or the doctor's expertise.

The U.S. Food and Drug Administration, the government body that tracks fertility clinics' standards, has a "whole laundry list of changes" clinics must comply with, Duke's Walmer explains. "It costs money to meet those standards." For example, 10 years ago it was OK for fertility doctor to use a catheter, which is used in animal husbandry to breed animals,

to inseminate women. This method was "just as good" as the instrument used to inseminate women today, but "regulation said you can't use in humans anymore," he continues. Catheters used in animals cost 10 cents; instruments used in women now cost 20 to 50 times this – or $2 to $5. Duke Fertility Clinic has had to hire staff solely to keep up with changes in regulation.

The Duke clinic's overhead cost includes four doctors and its lab in a stand-alone facility separate from Duke University's teaching hospital. The clinic also pays two staff members whose sole purpose is to explain insurance coverage.

A lot of instruments used in fertility labs – such as Petri dishes used to grow embryos, etc. – are sold in bulk. Markets dedicated to providing these instruments sterilized and ready-to-go. Duke Fertility Clinic will cut costs by not buying bulk sets all the time, but rather will buy instruments individually and sterilize them in house. "We constantly look at how we can be more efficient at what we do to keep costs down," Walmer says.

Fertility doctors operating high-tech labs, which are sterilized and have high standards of air quality control, so that the environment where the embryos grow and are transferred is just right. "It's very difficult to create an environment that produces the female reproductive tract," Walmer explains. "You have to do a lot of quality control."

"You're dealing with human embryos, and that's expensive," he continues.

When Mary went in for treatment at the Jones Institute for Reproductive Medicine in April 2007, she paid $11,200 for her egg retrieval, ultrasound, blood work, embryo transfer and a procedure called intracytoplasmic sperm injection. This is when one sperm is manually put into one egg. She also paid $400 in anesthesiologist fees and $1,620 to have her

remaining embryos frozen. She's unsure how much her second round of IVF will cost in July.

"This is not a system where people are trying to run the cost up as much as they can," Walmer explains. Clinics do several things to keep costs down.

First, doctors make sure patients' treatment is appropriate for their prognosis. For example, some clinics will give the fertility drug Clomid, which enhances ovulation, as a first-line treatment before going on to more complicated procedures. This process is often much cheaper than more complicated procedures such as IVF. When Mary took Clomid, it cost her less than $50 each month.

However, most in vitro fertilization procedures are not covered by insurance. Some states such as Arkansas, Connecticut and Maryland offer coverage, but the majority do not. Some insurance carriers will pay for initial testing to diagnosis infertility and at times will pay for some drugs.

Some clinics also offer shared-risk programs to help create insurance where there isn't any, Walmer says. For example, the Jones Institute for Reproductive Medicine offers some couples two to four rounds of in vitro fertilization for almost $20,000 with a 50 percent money back guarantee if the treatment isn't successful. The clinic has criteria based on "economic need and personal circumstances" that a woman must meet in order to qualify, according to the clinic's Web site.

Mary did not qualify for the Jones Institute for Reproductive Medicine's shared risk program because she has an antibody in her blood that complicates gestation and because she has had a rare ectopic pregnancy, when an embryo implants outside of the uterus.

As she proceeded with her treatment, she asked staff members point blank: 'I know y'all are obviously a business, but would you keep taking my money if you didn't think this was going to work?" The clinic staff replied, "Mary, if we didn't think it was going to work, we would not waste your time."

A Better Deal for Consumers

Although the cost of in vitro fertilization has not declined, doctors say consumers are getting better treatment with much better odds of success. Success rates have increased from 10 to 15 percent in the late 1980s to 50 percent in 2007. That means couples' odds have increased 230 to 400 percent with each monthly cycle of IVF.

"If you look at the cost to achieve, it's actually gone down considerably," explains Keye of William Beaumont Hospital. "The $10,000 to $12,000 is a much better deal."

Modern couples appreciate their return on investment.

"It's a 50 percent success rate, so I can't get down about it," Mary says. "I told the doctor – and I told them all – your priority in July is me. It's nobody else. I don't care; y'all can ship all the other patients away. We've got a job to do."

V: Conclusion

Several reasons exist why major media outlets, such as the *Los Angeles Times, The Washington Post, USA TODAY* and *U.S. News & World Report,* chose not to cover the evolution of in vitro fertilization's technology and its cost.

One reason for the lack of coverage in these two areas is that it is easier for newspapers and weekly publications to cover IVF in short spurts that focus on one advancement at a time. Another reason is that in vitro fertilization spins off into many other newsworthy topics, such as ethical or legal issues. IVF also must compete with other health topics such as cancer, heart disease and AIDS for news coverage. Other reasons are more practical, such as space restrictions or IVF not aligning with news values. What's more, the nature of the print industry is fast-paced and strained by declining print subscriptions, declining revenue, declining news staff and greater workload. Reporters, therefore, don't always have time to work on longer stories. Digging into the evolution of a technology or unveiling its cost takes time.

Times health reporter Shari Roan has covered IVF since the beginning. She's been a health reporter since 1982. "It's a very interesting and provocative field," says Roan, who has worked at the *Times* since 1990. In vitro fertilization is "an area of medicine with great advances in a short period of time." The field has revealed basic knowledge of reproductive function and biology in the last 25 years, she says. "We've had to watch very closely to keep up with it." Journalists have had to be real consumer watchdogs with IVF because of its potential for possible abuse.

This story has so many facets to it, Roan continues. It is such a rich story. “Infertility affects a lot of people,” she adds.

What’s more, in vitro fertilization is dealing with human life, notes Dr. David Walmer, chief of reproductive endocrinology at Duke Fertility Center, who was a source throughout this series of magazine articles.

Covering Scientific Advancements

Media outlets have done a thorough job covering IVF’s medical advancement one at a time. “There has been a lot of news out of this field,” says Roan. Health reporters say a number of topics caught their attention most.

In the 1990s, newspapers covered intracytoplasmic sperm injection, ICSI for short. “Biologically, that was such a revolutionary thing,” Roan says. When doctors figured out how to put one sperm into one egg, they literally nailed down when conception occurred, explains Dr. Gianpiero D. Palermo, the first doctor to master the procedure. What’s more, researchers who first mastered ICSI also discovered the different stages of how eggs mature.

The 1990s also raised questions about the number of embryos doctors should implant into a woman’s uterus. As doctors implanted more embryos, they also grappled with an increasing number of multiple births. “We gave that (debate) a lot of attention – is this good or bad?” Roan says.

In 2000, preimplantation genetic diagnosis also got a lot of media attention because of its potential for “use and abuse,” Roan notes, “Could that be used for inappropriate selections, like sex selection?”

Egg freezing has been a big story in recent years, Roan says. It has a huge sociological impact because women can prolong fertility. "The science (of egg freezing) isn't very good," Roan says. "But it's there."

"We've done a fair amount on the advancements of IVF treatments," agrees health editor Glenn O'Neal, who has worked with *USA TODAY* since 2000. For example, the paper has written about a woman who had cancer and underwent chemotherapy and then went through in vitro fertilization to have children.

USA TODAY is interested in stories that either change procedures performed in doctor's offices or change the knowledge base of its readers, says O'Neal. Small advances will not get covered.

Ethical and Legal Concerns

In vitro fertilization brings up ethical issues because it deals with the beginning of human life. "IVF indeed has been under the microscope more than others," explains Dr. Howard W. Jones Jr., who alongside his wife Dr. Georgeanna Seegar Jones was the first to perform IVF successfully in the United States. "I think that has to do with the fact that it deals with one of the mysteries of the world – the initiation of the human individual. Therefore, it has had religious implications, philosophical implications, public policy aspects and all those things that don't seem to apply to other procedures, having your colon removed for cancer or something like that because that doesn't deal with reproduction."

"The fact that it has dealt with reproduction has made it fair game for these various groups to talk about," continues Howard Jones, 96, who consults for the Jones Institute for Reproductive Medicine. "We've spent a great deal of time on the public policy aspect of it

because we've had people who protested what we were doing, and people doing a picket line outside of the hospital. So people had to cross the picket line to go in and be treated. And indeed," he continues, "When Elizabeth Carr was born there was a guy with a sandwich board … outside, walking up and down, that said, 'See me for the truth,' or something like that. And he was handing out pamphlets saying the terrible things we were doing."

In vitro fertilization has raised a lot of questions because it is a new way of becoming a parent, Roan explains. "I think readers are very interested in ethical issues," she continues. For example, older mothers having children raises questions about how old is too old, ethically, to conceive and care for a child?"

"I really think most people are interested in the moral issues or advancements," adds *USA TODAY's* O'Neal. He says his paper's readers are interested in advances that make IVF more efficient and diminish complications, followed by moral debates. "I think the moral issues – what we're doing with this technology – is a hot topic for us," he continues.

IVF has raised a lot of legal questions as well, such as who gets the rights to leftover embryos, the legal ins-and-outs of surrogacy or donor eggs, Roan continues.

"The law still struggles and is behind the curve," Dr. William Keye Jr., who was president for the American Society of Reproductive Medicine in 2000 to 2001.

Other aspects of IVF have also attracted attention. For example, a whole scientific discipline looks at the psychological impact of in vitro fertilization, explains Keye, who is the director of the division of reproductive endocrinology and infertility at William Beaumont Hospital in Royal Oak, Mich. A new textbook, "The Infertility Counseling," was released in 2006. The mere size of the textbook reflects interest, Keye adds. The book, written by Sharon

N. Covington and Linda Hammer Burns, was reviewed and recommended by the Mental Health Professional Group, a subgroup of the American Society for Reproductive Medicine.

President George W. Bush's Council on Bioethics board led by Dr. Leon R. Kass has spent a lot of time looking at IVF. This board has also paid close attention to embryonic stem cell research and what the government will and will not federally fund. "We've mainly looked at stem cell as a separate issue (from IVF)," explains O'Neal.

All of these aspects – ethical, legal and social – are an "important part of the history of IVF in this country," Keye adds.

Competing with Big Health Topics

Although in vitro fertilization is an important procedure in the United States, it has to compete with huge medical topics for news coverage – such as AIDS, heart disease and cancer. AIDS erupted as an epidemic in the 1980s and has received a lot of media attention. Heart disease is still the No. 1 killing disease in the country, according to the National Center for Health Statistics. More than 650,000 people died from heart disease in 2004, the last year mortality data are available. In 2004, 16 million citizens had a form of cancer at some point in their life.

"The health and medical field is very rich," Roan says. "There is so much out there to choose from. (*The Times*) is very picky. We go for the best stories."

"We don't write about tiny advances because we can't," Roan continues. She will read medical journals and the latest advancements of different medical fields, such as IVF, and stay on top of changes but she won't always stop and write a story about it.

The New England Journal of Medicine, *The Journal of the American Medical Association*, *The Lancet*, *The British Medical Journal* and a plethora of other medical journals are released every month, packed with medical advances, tips for procedures, opinions about each specific field and more. Journalists have a lot of information to evaluate.

"(IVF) is competing with every other medical topic under the sun," O'Neal agrees.

Constraints of the Health Desk

While managing a constant stream of health and medical information, reporters on a national health desk have to face space and time constraints – what the publication can feasibly cover.

"I have very little time to develop a very long, in-depth investigative piece," says Roan, who is the most knowledgeable journalist about IVF at the *Times*. "My position is not set up to do that," she says, "My job is set up to be productive."

On average, Roan writes three 30- to 45-inch stories each month for the newspaper's weekly magazine. "I don't really write many smaller pieces because of staffing."

The print industry has downsized to survive declining subscriptions, according to the American Press Institute. "With thousands of job cuts in recent years, costly news coverage that includes two foreign wars, and ever-escalating demand for Web content, newspapers these days are being forced to do more with less," explains Joe Strupp in his special report, published on June 3 in *Editor & Publisher.* The American Press Institute has started a seminar called Newspaper Next to help publications rethink their business strategy and bounce back. The overall industry changes mean reporters have to write and report quickly and help carry the weight of a lighter staff.

Some newspapers, like *USA TODAY,* have withstood industry changes. Staffing is not a problem, O'Neal says. He has six reporters on staff, two steady freelance writers and a few science reporters who will write about stem cell research, obesity or emergency medicine. Each week his staff writes six to eight news stories, which are seven to 14 inches, one to four center pieces, which are 20 inches, and at least one cover story each week, which is 25 to 35 inches. "It's difficult but often doable" to take on longer, more in-depth investigative pieces, O'Neal says.

But there are always more stories than bodies, time and space to cover, O'Neal says. "It's a constant battle."

Reasons Other Than Staffing

National newspapers and weekly magazines opted not to cover the evolution or cost of IVF for other reasons. "I think the science is of less interest to the public," Roan says. "The finer points of science." The *Times'* readers are more concerned with ethics.

Running a story that is 5,000 words, or roughly 125 inches, is "even difficult to get in The New York Times," O'Neal says. At *USA TODAY* "it would be next to impossible to get in, quite frankly."

"The cost over recent years has gotten a lot less coverage," Roan says. Most stories mention cost but that has gotten lost, Roan says. Usually with new technology, the cost is high at first and then comes down. But that hasn't been the case of IVF. "A lot of clinics have made a lot of good money," she says. Roan agrees the *Times* has not written about in vitro fertilization's bottom line.

The high cost is part of a larger picture, the cost of health care in general, Roan continues. “Now cost is an issue for everyone,” she says. “Cost has become a crucial topic.”

Future Coverage

The media has covered many aspects of IVF in the past 25 years, and it will continue to be fascinated with new developments as fodder for stories. *Times* heath reporter Roan believes preimplantation genetic diagnosis, embryo transfer guidelines, the debate about leftover embryos and increasing government regulation will be the hot topics in future news coverage. “The IVF field has been very loosely governed,” Roan says, and it may see more regulation.

According to wire reports, 3 million babies have been born worldwide from the reproductive technology.

Covering the development and cost of in vitro fertilization may be long overdue.

Appendix I:
List of Interviews

Cimuchowski, Heather. Modern in vitro fertilization patient. Phone interview. May 23, 2007.

Houck, Sarah Smith. First woman to go through in vitro fertilization at Eastern Virginia Medical School. In-house interview. March 15, 2007.

Jones, Dr. Howard Jr. Pioneer of in vitro fertilization in the United States. In-office interview. February 16, 2007.

Keye, Jr., Dr. William. Director of the division of reproductive endocrinology and infertility at William Beaumont Hospital and former president of the American Society for Reproductive Medicine. Phone interview. May 23, 2007.

Mary. Modern in vitro fertilization patient whose name was withheld. In-office interview. May 31, 2007.

O'Neal, Glenn. Health editor for *USA TODAY.* Phone interview. June 14, 2007.

Palermo, Dr. Gianpiero D. ICSI pioneer, director of assisted fertilization and andrology at the Center for Reproductive Medicine and Infertility in New York and Cornell University associate professor. Phone interview. May 24, 2007.

Roan, Shari. Health reporter for the *Los Angeles Times.* Phone interview. June 6, 2007.

Walmer, Dr. David. Chief of reproductive endocrinology at Duke Fertility Center. In-office interview. March 30, 2007.

Appendix II:
Interview with Dr. Howard W. Jones Jr.
February 16, 2007

(Note: This section is the transcribed interview with Dr. Howard W. Jones Jr. of the Jones Institute for Reproductive Medicine. Direct quotes are verbatim. Indirect quotes, including my questions, are paraphrased. Notes are also included in parenthesis.)

Jillian C. Canada: Can you tell me what the procedure was like in the 1980s?
Dr. Howard Jones Jr.: "First of all, prior to patients being excepted into a program, it was necessary to establish a laboratory and be sure that you had conditions that were reasonable for fertilization to occur. For instance, in 1980, there was a suspicion that you had to work in the dark because it was said the sperm in the egg had never seen light. And therefore, when we first started, we used infrared lights in the laboratory."

Canada: Really, I didn't know that.
Jones: "Well this is an example, of the type of things. It was not known exactly what the pH of the (medium) should be. We started out with a pH of 7.2; 7.4 turned out to be a better pH.

And the efforts to control that pH were interesting because Edward Steptoe for instance, used nitrogen in the abdominal cavity (for a) laparoscopy (Check spelling) for fear that carbon dioxide would change the pH. When we started, this seemed to me to be dangerous because I was aware of an aneurism that had occurred with air or nitrogen in the abdominal, and we were reluctant to that. So we had to determine whether or not carbon dioxide *really did* make a difference. So we deliberately used carbon dioxide from the first and found that in order to compensate for that, we used a Butler, special Butler medium that

we felt would maintain the pH in the aspirated, cultured medium – in the cultured medium, into which we aspirated the molecular content. We had a lot of buffer.

We didn't know what the effective temperature was, for instance. Edward Steptoe worked in England where the laboratories are traditionally colder than they are here."

Canada: How much colder?

Jones: "Well, they're ambient. So their labs would be in the 60s. Our labs were ten degrees warmer than that. We didn't know whether the, what the effect of the temperature would be. And it later turned out that one has to be careful not to be too warm. For example, one time we considered and experimented with having heating arrangements on the microscope stage, but that it turned out you can risk a little cooling but you can't overheat. So that … all of this had to be worked out."

"And I could go on as to the various problems that had to be solved. One of the early laboratory … clinical assistants, actually, he was a fellow at our university… He spent a lot of time on determining what the pressure was at the tip of the needle versus compared to the pressure that was exerted at the end of the needle …" paraphrase: he was looking at the pressure differential in suction.

"Also there was the story of the so-called Blizzard Needle, in which illustrates a point. You know, when we first started we adopted the British notion of going for the natural cycle. Because they had tried the use of Perganol in over a hundred tries, and it had been

unsuccessful in conceiving a living child with that technique. And they went back to the natural cycle. And were doing this for quite a while … and was familiar for what was going on… and he (Who is he?) suggested that we try with the natural cycle."

"This meant you had to estimate when a patient was going to ovulate. And that wasn't easy because the things we had to work with were urinary LH system, which was not as precise as the current technology. And we often did the laparoscopies in the middle of the night in order to accommodate this. But the March of 1981…"

"No, March of 1980 I guess it was. We had a very big snow storm – there was three feet of snow. And we had a patient that was scheduled for laparoscopy at 1 a.m. I left home at 7 o'clock that night with the snow and didn't get to the hospital until 1 o'clock because of the difficulty… And it was 5 a.m. before everybody that was necessary – including the patient – was able to get to the hospital. And when we laparoscoped her we were not surprised, but never the less disappointed to see the stoma in the ovary because she, obviously, ovulated. We had missed it … And it was suggested – and I really don't know who made the suggestion – that maybe it would be possible to irrigate around the ovary with salt solution, introduce the super-pubic aspirated cumuli. And maybe we could find the egg in the aspirate. And that we did irrigate around and aspirate and low and behold we found the egg. The point was, this was a freshly ovulated human egg, and I don't think anyone had ever seen one before. And maybe no one has seen one since. But the point was the cumulus was tremendous in size. And we estimated that it would not be possible to get the cumulus and the oocyte through the diameter needle that were currently using unless we sheered off or

greatly-compressed the cumulus. At that time, we did not know what the function of the cumulus was: We didn't know if the cumulus needed to be on there or whether when the egg was in M2 the cumulus had discharged its function and was no longer necessary. Anyway, as a result of that experience we got in touch with an instrument maker we had known at Hopkins before we came here – by the name of Kelly; he was actually the grandson of Howard E. Kelly, who made the Kelly Clamp. But at any rate, he developed for us a needle that was far bigger in diameter than the needle we previously used and it had certain characteristics, which we called the Blizzard Needle. With that needle…"

Canada: That's a good name.

Jones: "Yeah, it's a good name. With that needle our percent of aspirating eggs through the laparoscope were really improved." It later turned out that the cumulus … probably has completed its mission and is no longer necessary. Current practice now is to use a smaller needle and sheer off the cumulus.

"At the beginning, we did two mock cycles on each patient before we did the laparoscopy."

Canada: What do you mean by mock cycles?

Jones: "Well, that means we monitored them – not using any stimulation, now understand – but we had them on a basal temperature chart (Check spelling)." "We did the (To Come) urine test for LH, and we examined the cervical mucus and also the maturation index in the vagina in order to determine when the LH surge occurred. And then when we estimated the

beginning LH surge, we also kept track during that first cycle of the length of time between the beginning LH surge to ovulation because that was not known. Anyway, we monitored the patients for two cycles because patients vary a little bit, cycle to cycle. So it seemed like a good idea to know each particular patients quirks. And in order to try to identify the optimum time for ovulation.

So in that first year we did forty-odd laparoscopies. And we got I think it was 17 eggs that were fertilized and transferable, and we had no pregnancies. So we were disappointed, of course, in the inadequacy of the cycle."

"And during the Christmas holidays from 1980 and 1981, my wife Georgeanna, whose painting is over there, who died last year, insisted that we use ovarian stimulation. Because she had experience with it in anovulatory patients and had no problems with pregnancies and so forth. And thought that it could be used with ovulatory patients, which was contrary to what Edwards had thought. Because he had tried it and failed and said it shouldn't be used. Anyway, in the beginning of 1981 we started with the Perganol. But the dosage we used then, it was very modest. For instance, in Judy Carr the first patient that we had (a successful birth), she received only 7.5 ampoules ... That was the technique used for ovulation induction rather than ovulation enhancement, which a term I used before in patients who were ovulating. At any rate, she got pregnant; Judy Carr got pregnant and that first year, I think we had five pregnancies or something like that, using the controlled ovarian hyper stimulation, which turns out a technique that is still currently used."

"We used the laparoscopic approach, of course, until the vaginal technique became available, which we first used with abdominal transducers. And then finally the vaginal transducers came along. So there's been a tremendous change, of course. The patients who were laparoscoped were omitted into the hospital overnight. Later, we did the laparoscopy on an outpatient basis and the patient went home. But now, of course, it's an outpatient procedure entirely."

Canada: What was the time line, from when it went from overnight to more of an outpatient procedure?

Jones: "Well, I think we had that overnight arrangement for a matter of … '82. I think around '83 we shifted to an outpatient then. That's a guess on my part."

Canada: And then switching to transvaginal?

"Maybe in the '80s." Not sure. Need to check. "I'm not sure when that transition occurred."

(Notes: Recap

Paraphrase, decided to use Perganol in the beginning of 1981.) "January of 1981."

Canada: Can you describe what it was like for a patient when they came in the early 1980s?

Jones: "Well of course we monitored patients much more carefully then they're monitored now. They would be monitored them everyday. And we would have to monitor them with abdominal ultrasound. So they would have to have a full bladder. So that the patients would come in…And the reason the waiting room downstairs is as large it is because the patients

would have to wait until their bladder was full before they could be ultra sounded. So they would sit in there and drink water or Coca-Cola, or whatever it was – fluid – and then when their bladder was full they'd raise their hands and try to come in to be ultrasound. And that would be a daily occurrence – that we would do everyday, so that the patients go to know each other and were often formed friendships that lasted for life. (This) is in contrast to the present situation, where patient comes in one by one and they don't have any group activities like they used to have. It was much more of a group procedure in the beginning than it is now."

Canada: What made you decide to get away from that?
Jones: "Well it was a technological development. I mean the development of the vaginal probe was the reasonably known … you had to have a full bladder."

Canada: About when did that happen?
Jones: "That's awful hard to remember…" Not sure.

"I know that we were still using the abdominal probe when we moved into this building. That's why we built it, the waiting room as big as it is. And we moved into this building, I think, in '91." So it was subsequent to that.

"Women now come in individually. They can be ultrasounded at any time. We don't… we used to have to take their blood. When we finally shifted over to the blood technology, we took bloods everyday. Now ... we may take it five times during the course of

a cycle, something like that. The number of blood draws is greatly reduced. And it's a simple procedure, from that point of view."

Canada: Do you think that the patients are missing out on the old, group camaraderie?
Jones: "Well I don't know if missing out is the right word. But I do believe that in the times when the groups were together there was a spirit of adventuresomeness on the part of both the patients and the doctors because it was a new procedure. And I think everybody was excited about participating in this both at the patient level and the physician level. And that kind of has worn off now because it's kind of old hat. And it's just another way to get pregnant. From the point of the view of crossing the prairies, that's gone."

Canada: What are the biggest milestones of IVF over the past 25 years?
Jones: Controlled ovarian hyperstimulation. "That certainly was one." The use of the vaginal probe and its ability to aspirate the oocytes vaginally. "ICSI was certainly a big one." There have been modifications of culture technique, use of filters in the laboratory and other things that I regard as "important but minor" or not giant leaps like the things that I mentioned before.

Canada: What is the filter technology?
Jones: Air filtering. Positive pressure in the laboratory. Eliminating laboratory toxicity from whatever source.

Canada: What about the ability to freeze embryos?

Jones: “Freezing, yeah I suppose you could include that among the important things. That has been important. Yes, I think that would probably classify.”

Canada: Did couples in the ’80s approach IVF differently than they do now?
Jones: “I think early on everyone realized they were involved in an experiment. That they were prepared to participate in a sort of a procedure, the results of which were not clear as to whether they would get pregnant or not. Nowadays patients come in understanding that there is a procedure which will work but they also understand that it doesn’t always work. And that there is a definite percentage of success. That concept of there being a limit to what you could do was not present early on. We didn’t know about that. And that’s clarified.”

Notes: Pictures on the wall. From our very first patient. Not the first successful patient.
Jones: “Her name was Sarah Smith. She was a school teacher in Virginia Beach. She volunteered early on. And Sarah would do anything we wanted her to do. She understood and realized she was participating in an experiment. And we tried everything with Sarah. Following the … it occurred to us that maybe what we needed to do was let the patient ovulate and then with a needle puncture the cul-de-sac and put some salt solution in there, we would wash the egg out. Then we wouldn’t need to laparoscope the patient. Well we explained that to Sarah, and Sarah was willing to try that. She had that and tried; it didn’t work. We couldn’t find the egg. And we did a few other patients that same way. But Sarah was good for anything. So finally she got pregnant and she had twins.” And there the twins are (pointing over the wall) and here they are when they graduated from college.

Canada: And she got pregnant on her own?

Jones: "No, that was IVF." She had no tubes. "When we first started, we would take patients only if they had (no tubes) because we wanted to be sure that if they got pregnant, we knew they got pregnant by the process we were doing rather than have tubes that might possibly work. For the first year or so, all of the patients we had had (no tubes.)" "So these first patients were really patients that had tough histories. We didn't do normal infertile couples for instance."

Canada: Do modern couples approach IVF differently now?

Jones: "They understand all that. They are self-selected because they understood that, have read about, and know about that and are prepared to take that shot. In the early days, there was a frontier experience because nobody really knew how it was going be. They all were prepared to do that."

Canada: How have the attitudes of doctors in the medical community towards IVF changed in the past 25 years? Or has it changed?

Jones: "Well I'm not sure. Well I think at first there was a segment of the community, medical community, who thought this was a wild-haired scheme. And didn't think we could be successful. I've had none of that recently. Everybody realizes this is now an accepted medical procedure. I do think we are still in a process of evolution. I personally believe IVF should be used even more for frequently than it is now."

"In the United States for instance, about 1 percent of all newborn children are from IVF. In some of the other countries in the world – such as Scandinavia – it is up to 5 percent. So that IVF is used much more quickly in other areas of the world than it is here. In fact, the United States among the developed countries is the most infrequent user of IVF."

Canada: Really?

Jones: "The most frequent country is Israel followed, of all things, by Iceland. And this is probably related to the fact that there is insurance coverage in those countries." And this is true for many countries in Europe, "where insurance is available."

Canada: Do you think that IVF will be covered by U.S. insurance companies?

Jones: "I certainly think so. And one of the little projects (chuckle) I'm working on right now is trying to get the insurance company to realize. And this might come about if there is a certain, I call it, 21st century approach to the use of IVF. And that has to do with limiting the number of embryos transferred. In Belgium, for instance, they have a program which started in '03 where every patient is entitled to six tries. But if they are under 37 years of age, they can only have one (embryo) transferred or insurance wouldn't pay. And it's interesting what's happened there – the number of multiple births has really decreased."

"The insurance industry has got to understand what's happening elsewhere in the world and have policies which are consistent with the 21st century."

"The greatest incidence of multiple pregnancies is prematurely and therefore high cost is related to ovulation induction and ovulation enhancement, much more so than with IVF. So the insurance has go to do away with that procedure and use IVF."

Canada: What's the project that you're working on?
Jones: "We're working quietly with the insurance people. We're not having a public program."

Canada: What about the changes in cost? That's my second article. In the beginning of the early '80s the cost was around $3,000 but that's not including staying in the hospital. Now it's right around $10,000 to $12,000 per cycle. Do you think that cost of $3,000 in the early '80s was actually much higher? Has the cost of IVF stayed the same when you take in to consideration outside costs?

Jones: "Well of course the hospital costs have dropped down." And the … many programs have more in and out. They are getting ready to open a new facility in March; many programs (like Duke Fertility Center) already had that. "So that reduces the cost of the patient." "The drug costs represent a major portion of the cost of (IVF). And the cost in the United States for drugs is greater than it is in many other parts of the world." "This is a supply and demand problem that, I think, difficult for us to understand exactly." "If somehow the costs of drugs came down, we'd all be better off. But I don't see that happening in the near future. The drug companies have a bottom line, just like everybody else."

Canada: I'm going to talk to different drug companies and see why they cost what they do.
Jones: "I think it's just a market situation." Set the price at certain levels in different countries. "If you reduce the price here, then you have to go up somewhere else if the drug company is to make its money."

Canada: Do you think the fact that insurance in other countries covers the cost of drugs here but not here keeps the price up in the U.S.?
Jones: I don't think I understand the relation of the two. I think it would work the other way around. "If you're guaranteed, then that would keep the price up, I would think."

Canada: IVF industry is under the microscope and it's written about it a lot. There is a lot of regulation covering it and maybe not other procedures. Do you have any insight into that?
Jones: "Well I think that's a fact. I think IVF indeed has been under the microscope more than the others. And I think that has to do with the fact that it deals with one of the mysteries of the world – the initiation of the human individual. Therefore it has had religious implications, philosophical implications, public policy aspects, and all of those things that don't seem to apply to other procedures, having your colon removed for cancer or something like that because that doesn't deal with reproduction. The fact that it has dealt with reproduction has made it fair game for these various groups to talk about. And indeed … we've spent a great deal of time on the public policy aspects of it. Because we've had people who protested what we were doing and people doing a picket line outside of the hospital so people had to cross the picket line to go in and be treated. And indeed, when Elizabeth Carr was board there was a guy with a sandwich board … outside, walking up and down, that said

see me for the truth or something like that, and he was handing out pamphlets saying the terrible things we were doing." "So I do think IVF has been special in that regard."

Can you think of anything else to add?

All of the scientific things have been written up. Check the dates.

Notes: Getting lined up with Sarah Smith…"She was an experimenter." She was the first patient, ever at the Jones.

Canada: How did that come about?

Jones: We decided we were only going to take people without tubes. "We had thousands of people who wanted to come. So we just sorted through and obviously we took local people… And she came to the top of the list."

(Notes: Thank you…Follow-up questions are OK. Send Dr. Jones a copy.)

Follow-up Question, submitted via e-mail June 18, 2007:

Canada: I'm finishing my thesis for UNC-Chapel Hill and there was one figure I wanted to double check with you. Sarah Smith Houck and Dr. William Keye, who is a former president of ASRM, say that IVF cost about $5,000 to $6,000 in 1983. Does this figure seem accurate to you?

Jones: In stating costs for IVF, it's necessary to say what the costs include. Otherwise, it is not very meaningful. I believe it is accurate that an IVF cost in 1983 was about $5,000, but

this included everything, including drugs, medical care, etc. etc. In later years, costs have been prorated and are often given without drugs and without this and that, so that it is very necessary to know exactly what's included when you talk about costs.

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