



Amanda Lynn Catchings, first U.S. baby born by GIFT, with parents Christy and Gary.

By JOANNE SILBERNER

Mating rituals aside, the reproductive pathways in both males and females would seem to have been designed by contraption cartoonist Rube Goldberg. In a man, constant communication between testicular tissue and small glands at the base of the brain maintains the proper hormonal environment in the blood for spermatogenesis in the testicles; the sperm are produced in tubing within the testicles, then wind their way back up into the body and out.

In the woman, complex hormonal interactions stimulate the development of an egg that bursts from the ovary into the nearby fallopian tube. The egg slides through the tube, and if it encounters healthy sperm that have made it past the woman's cervical mucus and through the uterus, fertilization occurs and a few days later the developing embryo plants itself in the uterine wall.

As nature has it, only couples with everything in working order can make babies. About one in 10 U.S. couples are involuntarily childless. In women, infertility can result from a hormonal imbalance or other factor stanching ovarian function, or a fallopian tube made impassable by infection or surgery. Male factor infertility occurs when the sperm produced are low in vitality or number. And many cases of infertility can't be explained.

Modern science offers two conventional alternatives to nature's way: artificial insemination, which places sperm in the vagina or uterus; and *in vitro* fertilization, which brings sperm and egg together in a laboratory dish.

Within the last year, two new tech-

Babymaking: Expanding Horizons

For some couples the road to diapers and gurgles and midnight feedings can be a difficult one, especially when artificial insemination and *in vitro* fertilization fail. So researchers have come up with new and improved routes to conception.

niques have been added to the list: gamete intrafallopian transfer (GIFT) and transvaginal oocyte retrieval. The aim of both is to improve on the low success rate of *in vitro* fertilization — about 15 to 20 percent at best — with less trauma to the potential mother.

The GIFT procedure was devised by Ricardo Asch and his colleagues at the University of Texas Health Science Center at San Antonio. It is basically an attempt to mimic the normal physiological sequence of conception by bringing egg and sperm together in the woman's fallopian tubes.

The idea of GIFT, says Asch, is "to place things where they belong."

In getting both sperm and egg into the fallopian tube, GIFT goes one up on artificial insemination, in which sperm might not travel high enough up the fallopian tube, the egg might not be produced, or the egg might not make the jump from the ovary to the tube.

"There's a big filter in the female genital tract," says Asch. "Just a few sperm get to the cervix. Just a few of those get to the uterus. And just a few of those get to the tube." GIFT hopscoches past the blocks.

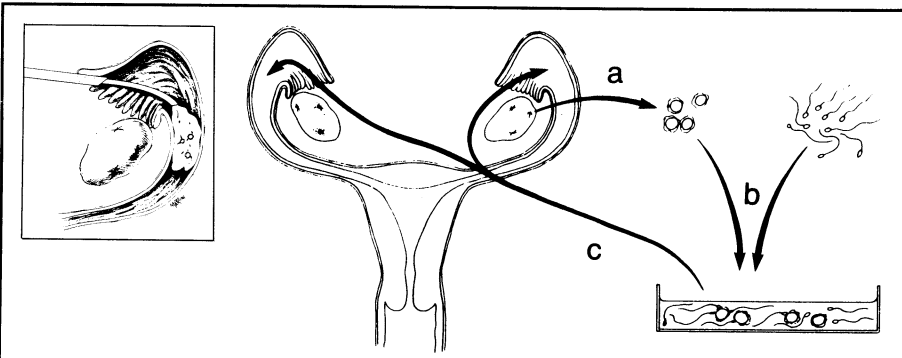
cision near the woman's navel; the incision is later sealed with a small adhesive strip.

Meanwhile, the potential father's semen has been treated to concentrate and stimulate the sperm.

Egg and sperm are mixed together and immediately inserted into the woman's fallopian tubes through the same laparoscope.

The advantage of GIFT over *in vitro* fertilization, says Asch, is that it allows the fertilized eggs to develop more before reaching the uterus — a closer parallel to what occurs naturally. In addition, it's a one-step process — the eggs are removed and reimplanted at the same time, through the same tube, rather than removed one day and reimplanted several days later as in *in vitro* fertilization.

About 75 percent of infertile couples could be helped by GIFT, Asch estimates. The treatment gets around the problem of unexplained infertility, which is a common "factor" for infertile couples, as well as poor sperm, certain ovulatory disorders, endometriosis and immunological and cervical factors. The GIFT procedure



In GIFT, a one-step process, eggs are removed from the ovaries, mixed with sperm in a lab dish and immediately placed in the fallopian tubes via a catheter (inset). With *in vitro* fertilization, time would have been allowed for fertilization and the eggs would have been implanted in the uterus a few days later.

"With GIFT we're avoiding the filters," he says.

As with conventional *in vitro* fertilization, the woman is primed with hormones to promote the development of several oocytes, and she receives a general anesthetic for the procedure. To harvest the eggs, Asch first sights them with a laparoscope, a fiber-optic viewing device fitted with a tube to suck up the eggs. The scope is inserted through a small in-

won't help women with blocked fallopian tubes.

Asch is also planning on investigating the use of only part of the procedure — putting sperm in the fallopian tube or removing and reimplanting the eggs.

The first GIFT gift occurred in April — twins born to a couple now living in Europe who wish to remain anonymous. Since then, says Asch, about eight GIFT babies have been born in the United

States and abroad. The pregnancy rate is 30 percent in about 500 tries, "much better than *in vitro* fertilization," he says. In a 20-country study begun in early 1985, about half of the institutions enrolled have already achieved pregnancies.

Asch says about 40 to 50 percent of the births have been twins. "We're in the stage of learning," he says. He may try putting fewer eggs back into the fallopian tube to solve the problem.

GIFT has a price advantage over *in vitro* fertilization. Because the eggs are removed and implanted in the same procedure, the cost is about \$1,500, compared with \$3,000 and up for *in vitro* fertilization.

The other new twist on fertilization is transvaginal oocyte retrieval, devised by Pierre Dellenbach of Centre Medico-Chirurgical & Obstetrical in Strasbourg, France. In transvaginal retrieval, a local anesthetic is injected in the vaginal wall, a needle is placed through the wall, and the needle's progress to the nearby ovary with its oocytes (nearly mature eggs) is monitored with ultrasound.

"At first we did our retrievals with laparoscopy, like everyone else," Dellenbach says. But then a patient came in

whose ovaries were hidden behind her uterus. Having read a paper from Copenhagen suggesting that oocytes could be recovered transabdominally — guiding a laparoscope across the abdomen, through the bladder and to the ovary, he and his colleagues decided a vaginal approach using ultrasound rather than direct visualization might be worth a try.

Following animal studies, they did their first retrieval at the end of January 1984; after five or six tries, and within a month, they achieved their first pregnancy. The first birth came in October 1984.

So far, 34 pregnancies have been achieved and 12 babies born at his clinic, Dellenbach said at a symposium on advances in human genetics and reproduction, held in Fairfax, Va., in October. The procedure is now common at *in vitro* fertilization clinics in Europe and is in use at several U.S. institutions.

The technique is not simple. The physician must make sure the woman is free of vaginal infection at the time of the procedure and must know the way around the pelvis to get the needle where it's going without hitting anything vital.

"It's been said that laparoscopy is easy for the doctor and difficult for the patient," says Dellenbach. "Our technique is

easy for the patient and a bit more difficult for the doctor."

Like GIFT, transvaginal oocyte retrieval is less expensive than *in vitro* fertilization — about half the cost, Dellenbach estimates. There's no operating room, no surgery, no anesthesia. "The patient comes in and goes out on her feet," he says.

The procedure, says infertility expert Luigi Mastroianni of the University of Pennsylvania in Philadelphia, allows recovery of eggs where it otherwise would be impossible — a situation another researcher estimates occurs in 5 to 10 percent of infertile women. Transvaginal retrieval has been done at Penn for about a year; it carries a slight risk of transporting bacteria to the ovary, but so far the danger is only theoretical, says Mastroianni.

"I think it's an exciting area and one with tremendous potential," he says. "We're very carefully monitoring our patients to be sure that it's equally safe [as *in vitro* fertilization]."

The Philadelphia institution plans to start using the GIFT procedure as well. "It's too early to say [GIFT] has an advantage over *in vitro* fertilization," he says. "But we already have a waiting list." □

Conceiving beginnings

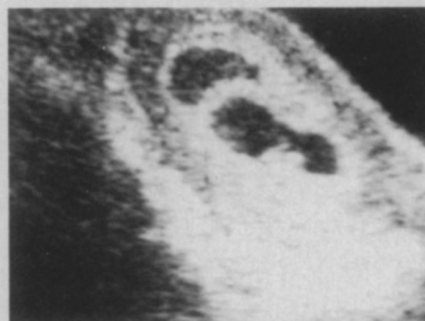
Joseph Schulman does transvaginal oocyte retrieval in a modern brown brick building in Fairfax, Va. Two couples sit in his plum-colored waiting room, one talking about the mild fall weather, the other silently leafing through magazines.

The receptionist takes a call from a patient who has just learned she is pregnant; the pleasure of the staff is evident in the voices that can be heard beyond the waiting room door. The couples in the waiting room don't seem to notice.

Schulman, who learned the technique from Pierre Dellenbach, has captained more than a dozen pregnancies since he started using transvaginal retrieval in late March at the Genetics and IVF Institute in Fairfax. "You really work hard for every pregnancy," he says. He has been able to retrieve oocytes (nearly mature eggs) nearly every time the attempt has been made, and has had a pregnancy rate of 30 percent per series of fertilized egg implants.

Today one of his patients is on her second try; in her previous cycle, fertility drugs caused a hormonal fluctuation that in turn may have prevented the pregnancy.

A day and a half before, the woman received a hormone to induce ovulation. Yesterday she douched to knock down the bacteria level in the vagina.



At top are three egg-containing follicles imaged by ultrasound during the procedure described here. The bottom ultrasound photograph shows the result, two tiny embryos growing in the uterus.

She now lies, mildly sedated, in a small room crowded with machines and what looks like a high-tech television.

Schulman inserts a speculum, and an ultrasound technician holds a microphone-like device over the woman's lower abdomen. To an uneducated eye,

the picture on the ultrasound screen looks like a very messy radar map, but when the microphone angle is adjusted several dark spaces appear.

The dark spaces represent what Schulman is after — egg-containing follicles, about 15 millimeters across. He anesthetizes the vaginal wall and inserts a needle, which can soon be seen on the screen drawing near one of the follicles. He pushes the needle to the follicle. As the needle enters the space, the follicle at first moves away, then gives in. Suction is applied to the needle and the dark space clouds up.

A syringe full of the suctioned-off fluid is quickly passed to the laboratory. A technician carefully disgorges the pink fluid from the syringe into a dish under a microscope. Nothing is there.

But in the next syringe, a tiny egg can clearly be seen with the naked eye. The technician moves a little more quickly. "A perfect egg," he says.

The process continues, with the needles and fluids kept on a warming tray, and the eggs placed in dishes in an incubator.

The harvested eggs will sit for several hours; then the husband's sperm will be added in a five-minute procedure.

In this case, five eggs are collected. All are fertilized, and at the woman's request, all are implanted. Thirty-two days later the results are seen — two little hearts flickering on an ultrasound screen. Twins.

— J. Silberner