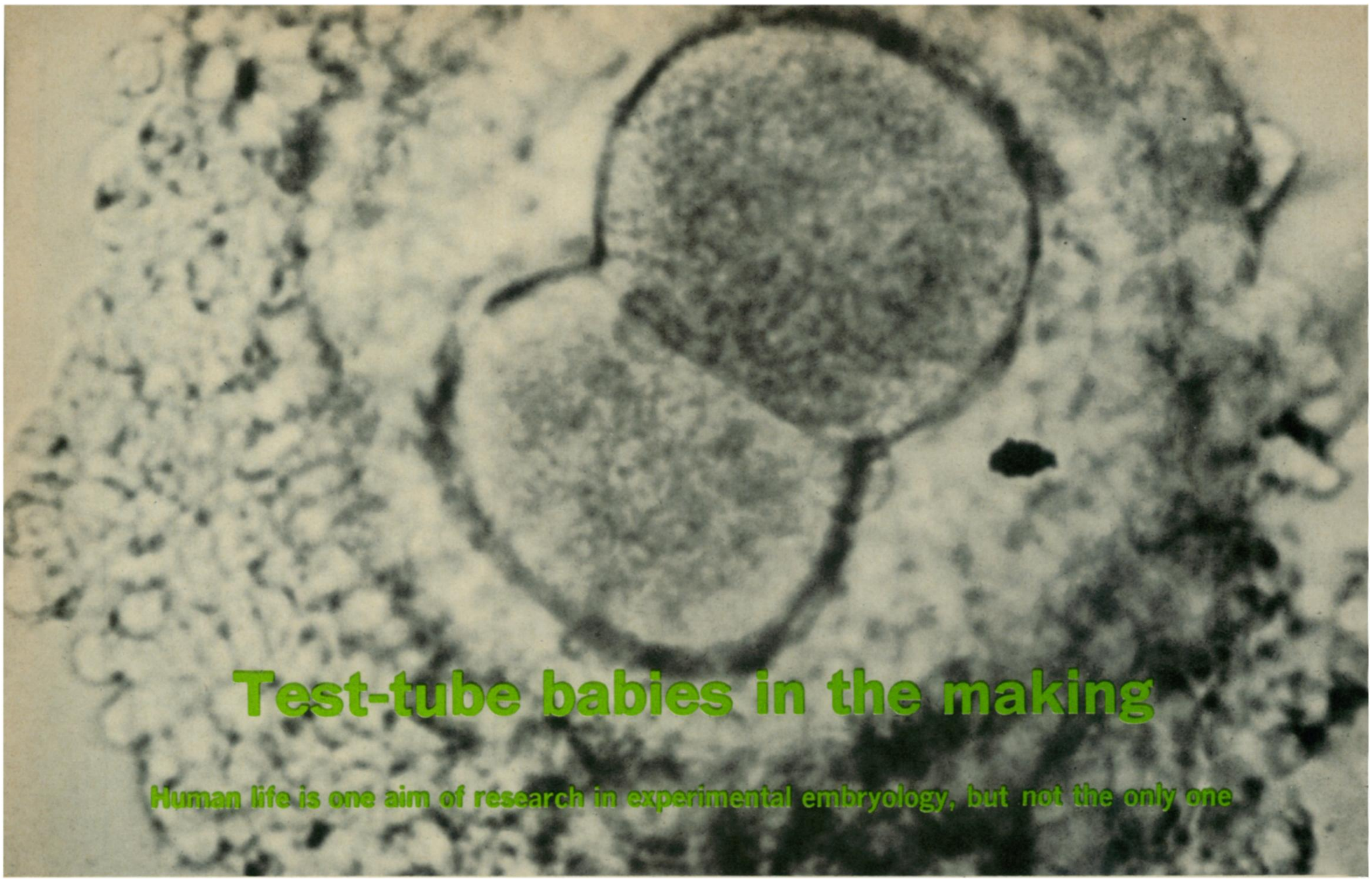


Test-tube babies in the making

Human life is one aim of research in experimental embryology, but not the only one

by Joan Arehart-Treichel

Laboratory lights glare down. Rubber-gloved hands glisten as they reach over the operating table and pluck out two ovaries, two oviducts and a uterus. The female organs are rushed to the Womb Room, a warm, humid chamber behind glass. There, eggs are flushed out of the organs and popped into a dish that contains sperm and chemicals. In three hours sperm penetrate the eggs. Within nine hours the eggs are fertilized, then divide into two cells, four cells, eight cells, sixteen. When they reach 16 cells or the blastocyst stage (where the fertilized egg is ready to implant itself in a uterus and become a fetus), the eggs are put into natural or substitute mothers who will carry them to birth. . . .

This is not a scene from science fiction, but a description of experiments now being conducted at the University of Pennsylvania School of Medicine on rabbits—and with ample success. Forty-four percent of the eggs taken from the ovaries of female rabbits and put into a culture dish with sperm become fertilized. Twenty-three percent of the fertilized eggs implant themselves in the uteri of female rabbits and result in live offspring. The Pennsylvania researchers are also fertilizing mice, with a 10 percent recovery rate.

During the past decade or so, not just rabbits and mice but also hamsters, guinea pigs, rats and cats have been fertilized outside the body. Only rabbits and rodents, however, have been carried to birth by natural or substitute mothers. Human eggs have also been fertilized by human sperm in the culture dish, but have not yet been implanted in a woman and carried to term.

Only a few researchers in England, Japan and the United States are working on making life in the lab. Their goals differ. R. G. Edwards of Cambridge University and Patrick Steptoe of Oldham General Hospital in England are trying to create human life in the laboratory. They first reported the mating of human eggs and sperm in the lab in 1969. They have since brought fertilized human eggs to the blastocyst stage. Word has it that they have collected several thousand eggs from women and may attempt to implant a fertilized egg into a woman any time now.

M. C. Chang of the Worcester Foundation in Shrewsbury, Mass., is probing the basic mechanisms of fertilization. His goal is to come up with ways to prevent sperm penetration that might be useful as a new kind of contraceptive. Since 1959 Chang has successfully fertilized in the lab rabbits, hamsters, mice and, most recently, rats. His in-vitro rats have also resulted in live offspring.

Pierre Soupart of Vanderbilt University in Tennessee is fertilizing human eggs and sperm in the lab, not to make human test-tube babies but to learn more about how human fertilization works. He wants to find a new means of birth control. The Belgian-born obstetrician usually stops human fertilized eggs at the two-cell stage so he can scrutinize their activity under the powerful electron microscope.

Benjamin Brackett and his team at the University of Pennsylvania are probing the intricacies of fertilization so they might come up with a new means of birth control. But Brackett, a biochemist-veterinarian, hopes to use laboratory fertilization primarily to reproduce more and better livestock. "The more animals we can produce," he attests, "the better can we meet world food needs." He visualizes fertilized eggs from exotic and popular breeds of cattle being carried to birth by Hereford cows. Laboratory fertilization, he believes, may also benefit the racehorse and show-horse industries. "Horses," he says, "have more trouble reproducing than any other domestic animal except man." Out-of-the-body fertilization may also offer clues for saving wildlife species that are threatened with extinction—the cheetah, for example.

In spite of their divergent goals these researchers are learning similar things about reproductive physiology and about the physical and chemical conditions that allow fertilization to take place outside the body. For example, temperature and humidity are crucial for making test-tube baby rabbits. Brackett worked in swim trunks for months until he got the temperature and humidity of the Womb Room just right. Mice, in contrast, can be reproduced in any room, in a culture dish placed on a hot plate.

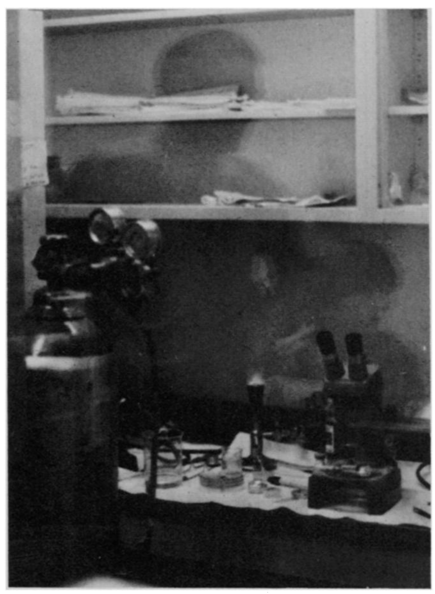
Certain chemicals must also be present if the sperm are to penetrate eggs in culture. Albumin is important, probably, Chang says, "because the sperm and eggs need some protein." Lactate, pyruvate and other nutrients normally present in living cells are also necessary. So is blood. So is sodium bicarbonate, which is normally present in the oviduct, where an egg is usually fertilized by a sperm. Brackett adds penicillin to the culture dish to keep bacteria from infecting eggs and sperm.

Chemicals in the female reproductive tract, probably in the oviducts or uterus, help sperm penetrate eggs. Sperm need the same or comparable chemicals to penetrate eggs in culture. Brackett's team used to use rabbit sperm that had already been primed (capacitated) by chemicals in the female rabbit. Now they have found that uterine fluids from the female rabbit can be placed in the culture dish to prime sperm there. Edwards and Steptoe say they use fluids from the ovaries to capacitate human sperm in culture.

Thanks to the electron microscope, many of the steps of fertilization in culture can actually be seen. Brackett and his colleagues also use a movie camera to record the events and play them back 90 times faster than real-life action. What can be seen with these techniques?

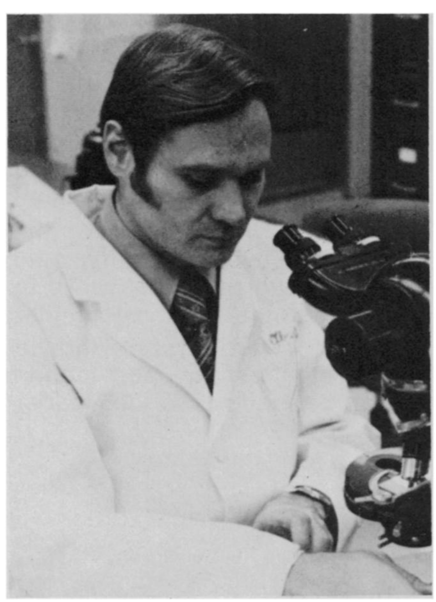
After an egg is ovulated, a little circle appears between the outer shell of the egg and the inner space of the egg. This "polar body" is a signal that the egg is ready to be fertilized. When an ovulated egg is placed in a dish containing sperm, the sperm swim to the egg and try to penetrate it. The sperm that gets in first is the winner. If the sperm is a rabbit sperm, it may tarry before moving into the center of the egg. If it is from a mouse, it immediately charges into the center. Once the sperm gets near the center, the sperm head enlarges into a male pronucleus. Female chromosomes already present in the center condense into a female pronucleus. The male and female pronuclei get bigger and come together. Their membranes dissolve; their chromosomes mix. The egg divides in two (see photograph opposite page, by Brackett in FERTILITY AND STERILITY). Each daughter cell gets

Hands cut, retrieve female organs.



Photos: Joan Arehart-Treichel

Organs are rushed to Womb Room.



Brackett examines lab-fertilized egg.

chromosomes from the sperm and from the egg. When the two cells divide, the four cells that result each contain chromosomes from the sperm and from the egg. And so on the process goes. This way the millions of cells that eventually become a living organism contain genes from the egg and the sperm.

No one is sure what constitutes fertilization. It may be sperm penetration. It may be penetration through egg cleavage into a blastocyst. When rabbits are fertilized in culture sperm penetration takes two to three hours and cell cleavage into a blastocyst nine hours. The events take about the same time if they occur in the oviduct of a female rabbit. For mice and humans, sperm penetration and cell division take a little longer, both in the lab and in the oviducts of female mice and women.

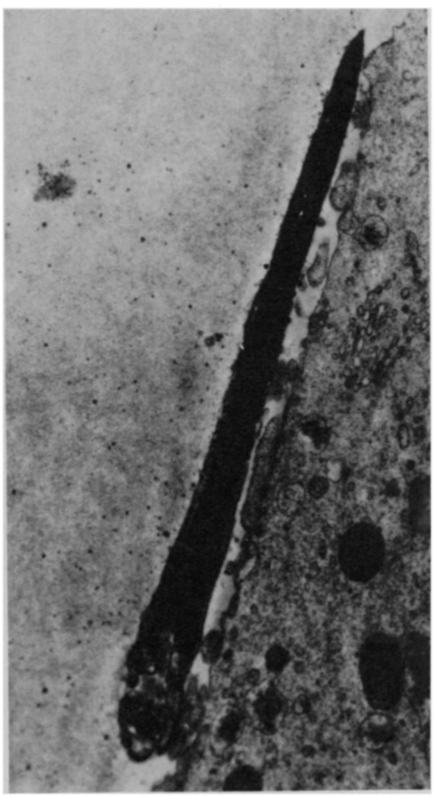
In spite of all they're learning, scientists doing laboratory fertilization must overcome some obstacles before they reach their goals. Edwards and Steptoe want to make sure that any fertilized human eggs they implant in women are normal. Some of the eggs they initially fertilized in the lab were not. They weren't sure whether their fertilization techniques were inadequate or the eggs themselves were defective. Brackett, however, says that the test-tube rabbits that his team has made have all been normal. Some have gone on to reproduce in the traditional manner; their offspring have also been normal. "These results," says Brackett, "may provide encouragement for human work."

On the other hand, the Pennsylvania workers are finding that the eggs with the best chances of being fertilized in culture are those that have just been released by the ovaries but that have not yet passed into the oviducts. "This is disappointing from the viewpoint of human fertilization," says Brackett. "It is easier to recover eggs from a woman's ovaries right before she ovulates."

As for using laboratory fertilization to get new kinds of contraceptives, Chang expects it will be some time before he finds a chemical that will keep sperm from penetrating an egg. Admits Soupart, "Making a lab fertilization system for human material operational is already a big proposition. We have that working now but the next step [making the eggs sperm-proof] is just beginning." Brackett and his co-workers have not yet figured out which uterine chemicals they use to prime sperm actually do the job. If they could, they might then learn how to block the chemicals. Blockage might be used for birth control.

Although lab fertilization researchers are producing test-tube rabbits and mice with consistency, they have not yet obtained such good results with other species. Monkeys are giving Brackett's group a particularly hard time. Brackett estimates it will probably be a few more years before livestock will be procreated in the lab.

Most people would probably approve of scientific efforts to improve livestock reproduction, save wildlife or to come up with better birth control. The idea of human test-tube babies, however, frightens or repulses many. Should scientists pursue this goal? "Absolutely," asserts Brackett, "not just for scientific achievement, but to help women with infertility problems conceive." Soupart agrees. "The classical application I can foresee," he says, "is where there is a physical block between where an egg is fertilized and where it implants, which cannot be solved by surgery; and the only way to overcome the problem is to take an egg out, fertilize it outside the body and put



Y. K. Oh, Univ. of Pa.

Sperm moves along outside an egg.

it back where it should implant later on." Soupart doesn't think that the technique would usurp traditional baby-making for the bulk of society.

Many are concerned, though, that the technique might be abused. For example, a woman might carry fertilized eggs that are not her own to birth, then sell the babies to couples who would pay a high price for them. Brackett also worries that the first culture-dish human baby "may not be done scientifically, but by some gutsy guy who does it the wrong way."

Regardless of what society thinks about human test-tube babies, it looks as if they're coming. Says Brackett, "It could be done now; it's only a question of when." □