In vitro Fertilization Goes Commercial

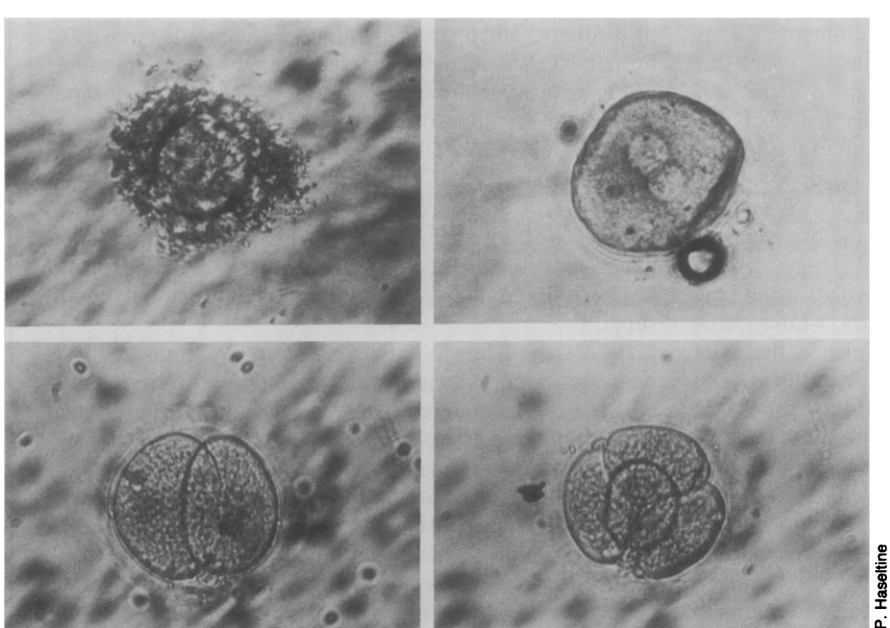
There could be as many as 200 clinics operating within a year; who should pay for the procedures, and how should they be monitored?

In vitro fertilization is rapidly moving from an esoteric technique to one that will be offered to the majority of the 1 million or so infertile women in this country who could possibly benefit from it. So far, only five medical centers in the United States have well-established programs. But, says Martin Quigley of the University of Texas Health Sciences Center at Houston, "Conservatively, I would estimate that at least 100 to 200 places are now doing it or talking of doing it in the next 12 to 18 months." Florence Haseltine of Yale University agrees. "They'll be coming out of the woodwork in the next few years," she says.

This rapid spread of the technique raises some important issues. How will patients know which groups are successful at this already chancy technique? What is a reasonable fee to charge? Who is going to pay? "The people who will suffer in the end are the patients," Quigley says.

Many insurance companies do not pay for the procedure, or pay for only portions of the medical costs, such as the hospitalization fees. Patients usually are charged $3000 to $4000 for each attempt and each attempt—at the well-established medical centers—has a 15 to 20 percent chance of success. Thus, it takes three attempts and $9000 to $12,000 for less than a 50 percent chance of becoming pregnant.

These success rates, however, are not constant. The established centers usually had no pregnancies at all in their first year of operation although, says Quigley, "I can't tell you what we're doing differently now than then." And all centers have what Quigley describes as "batting slumps"—periods when, for no discernable reason, none of their patients get pregnant. So a woman who goes to even an established center is by no means assured that she has a 15 to 20 percent chance of getting pregnant at each attempt.



F. P. Haseltine

Cleaving human egg

This embryo will be implanted into its mother's womb where, with luck, it will not be rejected.

Yet there is no shortage of people waiting to pay for the procedure. At Eastern Virginia Medical School in Norfolk, the first place in this country to offer in vitro fertilization, patients are scheduled 6 months ahead of time. And there are 3000 to 4000 patients waiting to get on the 6-month list. Since Eastern Virginia can only handle about 270 patients a year, this represents more than a 10-year backlog. However, says Howard Jones, who with his wife Georgeanna established the center 3 years ago at Eastern Virginia, many of these patients have their names on every waiting list in the country and many will be handled by the new centers that are springing up. "I don't know how alive that list is," Jones says.

The surfeit of patients, says Jones, is "an expression of the fact that [in vitro fertilization] can help a lot of people who can't otherwise be helped." The cost, although considerable, is not an overwhelming obstacle, Jones remarks, since, "a lot of people consider having a child a high priority item when it comes to doling out their budget." Joseph Schulman of the newly established unit at George Washington University School of Medicine, which recently announced its first pregnancy, says that he tells patients that the cost of the procedure pales in comparison to the cost of raising a child. "I tell patients to think of the $12,000 [it will likely cost them to get pregnant] as more like the cost of buying a car," he says.

Clearly, the long waiting lists at those places now offering in vitro fertilization have prompted many other groups to plan to offer it as well. But another factor is that the success rates for the procedure have finally reached an acceptable level. It took more than a decade of unsuccessful attempts before Patrick Steptoe and Robert Edwards of Cambridge, England, achieved the world's first "test tube baby" in 1978. Gradually, success rates began to improve, although no one has so far achieved more than a 20 percent pregnancy rate per attempt.

The reasons for the improved success are hard to pinpoint. Researchers cite experience, minor changes in methodology, and, as Schulman puts it, "A whole lot of witchcraft—a lot of little things we don't understand."

Everyone agrees, however, that it takes a large experienced team of 12 to 20 people to run a successful program. "It's very labor-intensive," Haseltine remarks. For that reason, the established investigators are concerned that some of the newcomers to the field may not be able to achieve anywhere near 15 to 20 percent success rates. Quigley says he is not so concerned about the centers being

established at medical schools. It is the private clinics that particularly bother him. One sent out fliers to obstetricians throughout the country claiming phenomenal success rates—with no documentation. Others are charging as much as $7000 per attempt.

The American Fertility Society has put together a committee, headed by Howard Jones, to set up minimal standards for in vitro fertilization teams. The society hopes to use these standards in order to determine which groups to recommend when patients ask for referrals. The committee believes a team should include a person with formal training in reproductive endocrinology, a reproductive biologist who is experienced in sperm and egg collection, fertilization and early cleavage in both humans and animals, a person with extensive experience in gynecological laparoscopy who is technically capable of getting eggs but who also is sufficiently experienced to recognize when tubal reconstruction is more appropriate than in vitro fertilization, and a person with experience in male infertility and egg handling.

The problem with the current uncontrolled, wide dissemination of the procedure, say the experts, is not only that some patients will be gouged. It is also that insurance companies are unlikely to recognize in vitro fertilization as an established treatment if most teams are inexperienced and unsuccessful. But, as has happened before, the medical profession is finding it very difficult to police itself.—**GINA KOLATA**

Dioxins' Health Effects Remain Puzzling

In vitro tests suggests it causes cancer, medical results remain ambiguous

The disagreement among researchers about the public health effects of dioxins is widening, judging from several papers presented during the national meeting of the American Chemical Society, held in Washington in late August. At one extreme, a study of U.S. veterans who served in Vietnam has found no unusual medical problems attributable to dioxin exposure. At the other, researchers studying dioxin toxicity reported that these chemicals are full-fledged cancer-causing agents, capable of initiating tumor growth as well as promoting it.

There seems little likelihood that these conflicting views can be reconciled anytime soon. Moreover, the scope of the dioxin health debate is widening in other ways: New York health officials have found dioxins not only in soot that resulted from a transformer fire but also in body fats of personnel who fought that fire and cleaned up after it. Some of those people appear to have suffered health effects, including chloracne and altered liver functions, according to Arnold Schecter of the Upstate Medical Center, State University of New York, Binghamton.

About 500 persons still are under medical surveillance because of that fire, which occurred in early 1981 and has since elicited more than $1 billion in law suits. Elevated levels of liver enzymes, triglycerides, and cholesterol were found in some of these 500 patients "without etiology being well characterized," Schecter says. Liver biopsies reveal that mitochondria of these patients sometimes take on "bizarre shapes" and that other abnormalities in liver cells are plentiful. "We think this is clinically related to chemical exposure," he says.

These patients were exposed not only to dioxins but also polychlorinated biphenyl compounds (PCB's), furans, and biphenylenes, Schecter points out. However, it has proved difficult to estimate exposure levels to those chemicals for various reasons, not the least of which is the problem of reliably measuring their residues in human tissues. Nonetheless, some of these patients have dioxins and other such chemicals at levels in the 8000 parts-per-trillion range in their body fat, he says. But, to further complicate this picture, analysis of control patients (typically, Binghamton area residents hospitalized for surgery) revealed that some of them also carry such chemicals in their body fat, the highest such reading being in the 2000 parts-per-trillion range, Schecter notes. Validating the degree of exposure to dioxins and other potentially harmful chemicals must be done so "epidemiology won't fall flat on its face," he concludes.

> "I believe dioxin actually has the ability to cause cancer itself . . . rather than being merely a cancer promoter."

The difficulties encountered by Schecter and his collaborators in following a modest-sized population are meager compared to those facing the Veterans Administration team that is looking at 85,000 veterans of the Vietnam War. These veterans are a "self-selected" group, who voluntarily have reported back to VA hospitals in the belief that their medical problems might be attributable to exposure to the herbicide Agent Orange, according to Alvin L. Young of the VA's Agent Orange projects office. That herbicide, which contained dioxins as contaminants, was used to defoliate the Vietnamese countryside during the war. Within this large group of veterans who have come in for the Agent Orange registry exam, according to Young, about three-quarters of them did not know whether they had indeed been exposed to the herbicide or what the extent of that exposure was.

"Nothing stands out—nothing confirms any specific Agent Orange effect," Young says. Instead, the health patterns of those Vietnam veterans so far resemble those of similarly aged men "growing older." Incidence of cancers within the group also is not unusual, he says. Critics point out that, because it is so difficult to establish what constitutes a proper control group, conclusions about incidence are extremely difficult to reach and potentially misleading. Young, who agrees that this medical surveillance of such a vast group is fraught with problems, says that the more definitive Ranch Hand study will be released early in October. This is a "carefully matched