# Britain's Lords Debate Embryo Research

*A bill in Parliament could ban research on human embryos, crippling attempts to improve IVF and early genetic screening*

URGED ON by anti-abortion groups, Britain's Parliament is considering an outright ban on all research involving human embryos. Unlike the U.S. ban, which covers only federally financed fetal research, the British one, included in a measure recently introduced into the House of Lords, would bar all fetal research. If the ban is approved, the research most directly affected would be work aimed at increasing the success rate of in vitro fertilization (IVF) and at improving methods of genetic screening.

Since the proposed bill does not ban IVF, its passage could create a situation in which IVF is carried out without the research needed to improve it. Curiously, the bill would allow untried procedures to be carried out on an embryo—as long as it is replaced in the mother and carried to term. But that exception hasn't brought cheers from the British scientists who do research on IVF or genetic screening; most are deeply disturbed by the possibility of a ban.

All IVF and research on human embryos in Britain is currently regulated on a voluntary basis by a body called the Interim Licensing Authority. The Human Fertilisation and Embryology Bill, first debated last week in the House of Lords, would replace the interim body with a compulsory Statutory Licensing Authority and impose criminal penalties for violations.

The bill offers members of Parliament a choice between alternative versions of the key clause. One permits research on embryos up to 14 days old; the other bans such research altogether. Some British researchers fear Parliament will opt for the ban. Alan Handyside of the Royal Postgraduate Medical School in Hammersmith, whose work deals with early detection of abnormal embryos, thinks there is "a majority . . . in Parliament who are not really in touch with medical research." That majority, Handyside says, believes ongoing research is not paramount because medical procedures work well from the first time they are performed.

Scientists like Handyside, on the other hand, believe research to improve IVF methods is desperately needed, a need partly dictated by the relatively low success rate of IVF. That rate (sometimes called the "take-home baby rate") is currently about 10%. The high failure rate is due to the number of steps that intervene between ovulation and delivery. Although collecting and fertilizing the eggs is often quite successful, at implantation and afterwards the failure rate is high.

As a result, most IVF clinics resort to "superovulation," in which a woman is given a combination of hormones to increase the number of eggs produced in a single cycle. Of, say, six eggs extracted and fertilized in a petri dish, three or four are picked for implantation in the hope that at least one will survive to term. Available methods for selecting viable embryos are "notoriously imprecise and subjective," according to Henry Leese of York University, whose work centers on developing objective criteria for choosing the embryos most likely to survive to term.

Leese's group has developed assays of embryonic metabolism based on how much nutrient the embryo takes up from the culture medium. Previous work suggests such metabolic indices may be correlated with viability, and the method is now in clinical trials at IVF clinics at the Hammersmith Hospital in London and the Sheffield Fertility Centre in Yorkshire. "The early results . . . are encouraging in showing differences between those embryos that give a pregnancy and those that do not," Leese says.

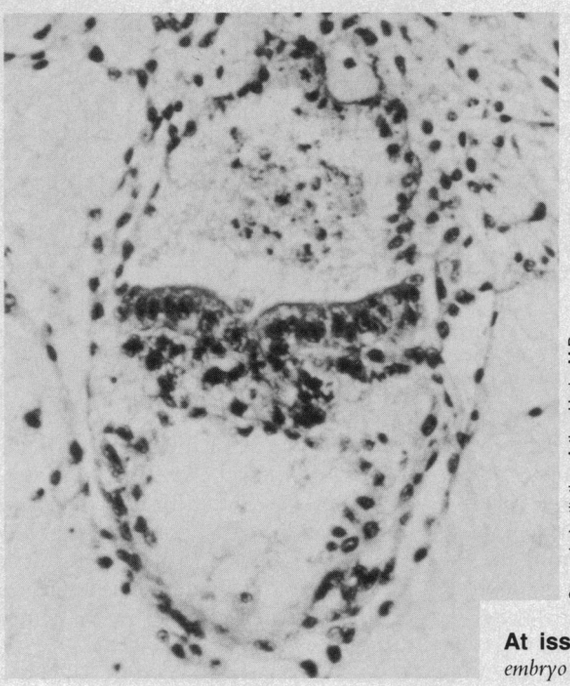
Curiously, although much research on IVF might be banned if the bill passes in its stringent form, Leese's own work might survive. The bill allows assessment of the suitability of embryos for implantation but mandates that every embryo must be returned to the mother. The result, as Handyside derisively puts it, would be to make "not only the embryo but the mother the guinea pigs of any new treatment. That's very bad medicine."

Forms of research that would not be offered even this narrow loophole include work on genetic screening, which would suffer precisely because its aim is detecting those (defective) embryos that should not be implanted. Handyside is one of those carrying out such research. He is concentrating on experimental methods for removing a single cell from an early-stage embryo and using the polymerase chain reaction to amplify the cell's DNA enough to detect genetic defects.

The work that has already been done on this method suggests that this kind of biopsy does not affect the subsequent development of the embryo. If the method proves to be not only safe but consistently accurate, it could have significant benefits for at least two groups of women. The first group is women with fertility problems, who are currently the main users of IVF. For them the risk of carrying a genetically defective fetus to term would be reduced.

The second group consists of women who have already had a child with a genetic disease such as cystic fibrosis and opted for tubal ligation rather than risk experiencing the same trauma a second time. Such women would be "ideal patients for an IVF approach," Handyside says.

They could choose IVF with the guarantee that only embryos without the gene for cystic fibrosis would be implanted; they could then become pregnant without having to have the tubal ligation reversed. To make such an approach possible, Handyside has been working with Robert Williamson's group at St. Mary's Hospital Medical



Carnegie Institution, Arthur Herig, M.D.

**At issue:human life.** *A 14-day human embryo in cross section.*

School in London to develop a polymerase chain reaction–based test for the cystic fibrosis gene.

But advocates of the new bill are unswayed by the potential benefits of such research. Jack Scarisbrick, director of Life, Britain's largest anti-abortion group, says that researchers "want to have embryos in order to detect chromosomal and genetic disorders, not primarily in order to cure them . . . but to be able to detect these defects and to kill them."

As Scarisbrick's use of the word "kill" suggests, the debate on the bill in Parliament, like the abortion debate in the United States, turns largely on the moral issue of when life begins. Those who favor the less stringent version of the bill—the one permitting research on embryos up to 14 days—do so on the grounds that before that time an embryo can hardly be considered "human."

Fourteen days was chosen because it is only at that time that the "primitive streak" appears. The primitive streak is the first group of cells that will go to make up the embryo itself. Until the primitive streak forms, almost the entire conceptus (the sum total of tissues derived from the fertilized egg) consists of membranes, such as the placenta, that ultimately provide support for the developing embryo.

Even a cutoff of 14 days is so late as to be theoretical, given the available techniques for dealing with human embryos. Few investigators have kept a human embryo alive in the laboratory even until the ninth day after fertilization. In most laboratories day 6 or day 7 is the usual limit.

But, as in the United States, British "pro-life" forces believe human life begins at the instant of conception. John McLean, lecturer in anatomy at Manchester University and an adviser to the pro-life members of Parliament, says, "I am convinced . . . that life does begin at fertilization." Experiments on embryos, even before 14 days, "threaten the lives of the subjects," McLean says.

Scarisbrick concurs. "A civilized society," he says, "must not use human subjects without their consent for research and experimentation which results in them being mutilated and killed."

It will take some time to determine which of these opposing views will prevail. After being debated in the House of Lords, the fertilization bill has now been sent to committee. From there it will emerge to be debated again and then passed along to the House of Commons. No one can say for certain when it will see the light of day again, but some observers predict that it could happen as soon as February.

■ JEREMY CHERFAS

# Science and PR North of the Border

*Were unpublished scientific results used as a weapon in the battle to take over Canada's premier biotechnology firm?*

THE UNITED STATES is not the only North American country where the takeover of high-tech firms by foreign corporations generates high stakes—and complex issues in science. Last week a government decision cleared the way for Connaught BioSciences Ltd., Canada's premier biotechnology company, to be sold to Institut Merieux, S.A., of France, ending a complicated takeover attempt that began in mid-1988. One of the many twists and turns along the way was an attempt by Chiron Corp., the American biotech company, to place a story based on unpublished results of its AIDS vaccine research in the Toronto *Globe and Mail*, one of Canada's best known newspapers.

Chiron, with its Swiss partner, the pharmaceutical giant CIBA-Geigy, was competing with Merieux for Connaught. The AIDS vaccine article, reporting promising preliminary results of a phase I clinical trial, appears to have been an attempt to sway public and government opinion in Chiron's favor. Editors at the *Globe and Mail*, fearful of being used, killed the story. But—like the cold fusion case—the episode raises sharp questions about the appropriate use of data that has not been peer-reviewed.

Connaught was founded at the University of Toronto in 1914 and its commercial success was established by production of the first commercial insulin for treating diabetes. The company is currently one of the world's largest vaccine makers, producing vaccines against polio, meningitis, and influenza, among other diseases.

In recent years, as clinical trials have become increasingly expensive, Connaught found itself hard pressed to muster the resources for developing new products and moving them to market. A report prepared for the Canadian government described Connaught as a "shrinking niche player" in the vaccine arena. The company's production and marketing facilities, however, made it a desirable target for a takeover. Enter Merieux.

In April 1988, Merieux first bid for Connaught shares, a move blocked by the securities commissions of Ontario and Quebec. A year later Merieux proposed to merge their vaccine operations with Connaught's, forming a new company based in Holland. Connaught's shareholders were not much interested because the deal would have given them stock in the new venture rather than cash. Two weeks before Connaught's board was to have voted on the offer, CIBA-Geigy and Chiron entered the picture.

CIBA-Geigy and Chiron made an offer of $30 (Canadian) per share for Connaught. Their bid also included a provision to make Connaught the headquarters of a new worldwide vaccine company—a provision aimed at reducing Canadian anxiety that, if Connaught were sold to a foreign concern, the once proud research facility would be turned into little more than the local marketing arm of an international giant.

Such considerations are not merely theoretical, because in Canada a federal agency called Investment Canada must approve any takeover by a foreign institution. That agency's standard for approval is whether the takeover provides "net benefit" to Canada. In the Connaught case the maintenance of an integral company, including research and development facilities, was apparently part of the overall "net benefit" package.

Investment Canada found the first Merieux cash offer unacceptable on "net benefits" grounds and the presence of a competing offer from CIBA-Geigy and Chiron made it possible to negotiate better terms. The negotiations were fruitful: Merieux came back with a bid of $37 per share that included an increased commitment to keeping research and development in Canada. That was where the story stood early this month, as Investment Canada pondered the two competing bids.

Chiron's bid—$30 a share—was lower than Merieux's, but intangible factors were part of the decision, and certain intangibles seemed worth emphasizing. One of them was the American company's research competence. A week before Investment Canada made its decision, Chiron contacted Geoffrey Rowan, a technology reporter for the *Globe and Mail*. Rowan was given some results of a phase I trial of an experimental AIDS vaccine, a trial that has not yet been described in a peer-reviewed context.

The results were hardly conclusive, but