SPECIAL REPORT

Ethicists and biologists ponder the price of eggs

A shortage of human eggs hinders stem-cell research. Paying women to donate would increase supply, but experts are divided over the merits — and the long-term health consequences — of such a policy.

H. MORGAN/SPL

Should women be paid for the time, discomfort and health risks involved in donating eggs for research? The world's largest group of stem-cell scientists is grappling with the question, and has now asked the public for its views.

Stem-cell researchers want eggs so they can work on somatic cell nuclear transfer, or 'therapeutic cloning'. They hope to derive embryonic stem cells matched to patients' DNA, by transferring the nucleus of one of the patient's cells into a human egg and developing it into an embryo from which cells can be derived. The technique has great medical potential — but researchers are far from achieving it, and the main limiting factor in the research is the availability of human eggs to practise on.

So far, scientists have relied on women already undergoing fertility treatment donating their extra eggs for research. But the supply is meagre. To help persuade them, several labs are increasingly offering financial rewards, such as cheaper fertility treatment. Others are starting to ask healthy women to donate — triggering a debate about how such women should be compensated.

Some ethicists argue that women should receive compensation for the discomfort and effort involved. Others are worried that this will create an undue incentive that will coerce women — especially poorer ones — into giving up their eggs. The fact that so little is known about the long-term health risks of the procedure further complicates the picture (see 'Health effects of egg donation may take decades to emerge', opposite).

Scientists in many parts of Europe, Asia, the Middle East and North America ask women to donate eggs for research, but they all treat the practice differently. Scientists at the North East England Stem Cell Institute announced on 27 July that they had got permission from the UK Human Fertilisation and Embryology Authority to pay part of the cost of *in vitro* fertilization treatments for women who donate eggs for research (see *Nature* 442, 498; 2006).

But other European countries that accept egg donation for research, such as Sweden, prohibit payment for anything other than direct expenses. Japan bans egg donation altogether because of the risk of complications, whereas China, along with several other countries, does not specifically address the question.

In the United States, a National Academies panel recommended last year that women should be reimbursed only for direct expenses. This approach has been adopted by the California Institute for Regenerative Medicine, and by the state of Massachusetts, home of the Harvard Stem Cell Institute (see *Nature* doi:10.1038/news060605-6; 2006). Both institutes are asking healthy women to donate eggs for research. But even their policies differ — for instance, California law would allow paying the travel expenses of women who come from out-of-state to donate eggs, whereas it's not clear how Harvard will handle this question. "At the moment we're confining the search to this area," says spokesman B. D. Colen.

Scientists want international guidelines so that they can share materials without worrying about how they were derived. So a task force of the International Society for Stem Cell Research (ISSCR) is considering the compensation question as part of a larger effort to draw up guidelines. The task force, made up of scientists, ethicists and lawyers from 14 countries, was convened last year after the revelation of scientific misconduct by South Korean stem-cell researcher Woo Suk Hwang: as well as faking evidence of 11 human embryonic stem-cell lines derived by therapeutic cloning, he lied about paying hundreds of women for eggs, and

Research volunteers or organ donors?

Much of the disagreement on compensation has arisen from the question of how egg donors should be viewed. Laurie Zoloth, a bioethicist at Northwestern University in Evanston, Illinois, who was on the ISSCR task force, argues that egg donation is similar to organ donation, and should therefore be free of financial considerations.

"One is asking the donor to undergo hyperstimulation, anaesthesia and minor surgery, then in a very real sense participate in the act of creation of an embryo that will be destroyed for research," she says. "This is a serious moral gesture, and I think it ought to be directed by a serious and reflective moral decision."

The eggs are to be used for research rather than medicine — but, Zoloth argues, so were the first organ donations. If scientists start paying for eggs now, she says, it will be difficult to stop payments once the technique moves to the clinic.

But bioethicist Insoo Hyun of Case Western Reserve University in Cleveland, Ohio, who was also on the task force, argues that egg donors should be treated as research volunteers, like those who donate bone marrow for research (see Commentary, page 629). Such participants are generally reimbursed for their time and discomfort.

Meanwhile, Kevin Eggan of the Harvard Stem Cell Institute, who was not a member of the task force, has another concern. Although avoiding compensation may reduce the risk that women could be coerced into donating eggs, it would also restrict the practice to wealthy donors, who can afford child care or to take time off work. The eggs upon which research is carried out would therefore represent only the most privileged groups, and not the population as a whole. "I think it's very hard to hold the line that reimbursing for minimal expenses is the right thing to do for the women involved," he says. **E.C.**

Mixed blessing? Donating eggs is a time-consuming and uncomfortable business.

obtained eggs from his female subordinates.

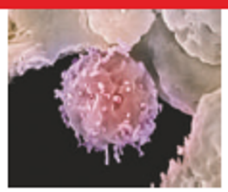
On 30 June, the ISSCR task force released draft guidelines at its annual meeting in Toronto. The guidelines embrace most of the principles proposed by the National Academies last year. But they differ on the issue of egg donation. The task force leaves the door open for a more liberal policy on compensation by stating simply that stem-cell research projects should be reviewed by a local oversight body, which must ensure "there are no undue inducements or other undue influences for the provision of human materials". What constitutes 'undue' is left to the local oversight bodies.

George Daley, a biologist at Harvard Medical School who chaired the task force, says that this is the best consensus the task force was able to achieve, because scientists and ethicists on the task force disagree so sharply about how egg donors should be treated (see 'Research volunteers or organ donors?).

The guidelines are seen as an important first step nonetheless, and are now open to public comment until 1 September, when the ISSCR will finalize the document.

"These are going to be seen as the rules set by scientists themselves, from the inside out," says Kevin Eggan of the Harvard Stem Cell Institute. "It's very useful for scientists to show that they have thought about these issues." ■

Erika Check



S. G. SCHMEISSNER/SPL

DISCUSS
The pros and cons of egg donation on our Newsblog
http://blogs.nature.com/news

Health effects of egg donation may take decades to emerge

In 1989, a healthy 32-year-old woman offered her infertile younger sister some of her healthy eggs, and with them the chance to have a baby. Doctors at the Cromwell IVF and Fertility Centre in London gave the donor hormones that made a batch of eggs in her ovary mature, and collected six eggs for fertilization. Three embryos were transferred to the younger sister and two were frozen. One baby girl was born.

Five years later, the doctors contacted the egg donor to ask whether to discard her frozen embryos. They discovered that she had been diagnosed with late-stage colon cancer that spread to her skull. She died just before her thirty-ninth birthday.

Doctors don't know if the fertility drugs caused or accelerated the woman's cancer. But the possibility prompted Cromwell infertility specialist Kamal Ahuja to report the case as a reminder of how little is known about the risks of donating eggs (K. E. Ahuja and E. G. Simons, *Hum. Reprod.* 13, 227–231; 1998). "It shook us all up," he says.

Specialists in reproductive medicine say there is insufficient information about the long-term risks of drugs used to stimulate ovulation, a practice that has become more common in the past 25 years, with the proliferation of *in vitro* fertilization (IVF) and assisted reproduction. But some studies have suggested the drugs may be linked to the development of certain cancers.

The question is receiving renewed scrutiny now that scientists are asking healthy women to donate their eggs for stem-cell research — exposing them to the potential risks of ovulation stimulation without the end result of a baby (see Editorial, page 601). To discuss the issue, the California Institute of Regenerative Medicine (CIRM) in San Francisco has convened a meeting of experts to be held next month. Britain's Human Fertilisation and Embryology Authority (HFEA) will also tackle the issue in a forthcoming consultation on egg donation for research.

The uncertainty makes it even more difficult to reach a consensus on whether women who donate eggs should be compensated, and if so by how much (see 'Ethicists and biologists ponder the price of eggs'). "This discussion should emphasize long-term risk assessment rather than money," Ahuja says.

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During ovulation stimulation for IVF or egg donation, women are given drugs that encourage the ovary to ripen several eggs simultaneously, rather than the one egg normally ovulated each month (see 'What egg donation involves', overleaf). Doctors know that this can have side effects ranging from moodiness to infection. The most serious is ovarian hyperstimulation syndrome, which seriously affects about 6% of women receiving the drugs. Thirty or more eggs start to develop at once and fluid leaks out of blood vessels and collects in the abdomen, causing nausea, bloating and very occasionally kidney failure or even death.

There is little information on how frequently ovulation stimulation has tragic side effects, says obstetrics and gynaecology professor Didi Braat of Radboud University Medical Centre in Nijmegen, the Netherlands, because doctors are often reluctant to report such cases and rarely have to. But deaths are thought exceptional: in a study reported at this year's meeting of the European Society for Human Reproduction and Embryology, Braat and her colleagues found only six deaths clearly linked to IVF from the medical records of some 100,000 women who underwent the procedure between 1984 and 2006.

So some specialists are more worried about the long-term risks of fertility drugs. In the 1990s, for example, studies pointed to a link between fertility drugs and breast or ovarian cancer, although it's not clear how cancer would be promoted. One study suggested that women who took an ovulation-stimulating drug called clomiphene citrate for more than a year had 11 times the risk of developing ovarian tumours compared with the general population (M. A. Rossing *et al. N. Engl. J. Med.* 331, 771–776; 1994).

But these studies are controversial. It might be infertility, not fertility drugs, that predisposes women to disease. Other aspects of women's reproductive lives influence ovarian and breast cancer — pregnancy is thought to protect against tumours, for example. And ovarian cancer is so rare that it's hard to get a large enough sample to spot any connection.

Louise Brinton at the US National Cancer Institute in Bethesda, Maryland, and her colleagues tried to control for these factors in one