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Today: Partly sunny,
warmer. High 76. Low 58.
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Stem Cell Discovery Grows Into A Debate

*New Field Faces Tests
On the Hill, in the Lab*

By RICK WEISS
Washington Post Staff Writer

It has been a year since researchers announced they had discovered in human embryos and fetuses a unique type of cell with the potential to treat a host of ailments, including diabetes, Parkinson's disease and even paralysis caused by spinal cord injury.

Now, in the final weeks of bargaining over a new federal budget, a divided Congress is struggling to decide whether the medical promise of these "human embryonic stem cells" is great enough to justify the use of taxpayer money to study them, despite the fact that embryos and fetuses must be destroyed to get them.

Congress has blocked federal funding of human embryo research for the past four years, but the discovery of stem cells has upped the ante in the embryo research debate. The research ban, which is attached to the appropriations bill for the departments of Labor and Health and Human Services, underwent several radical changes while the Senate addressed the bill last week, at various times containing prohibitions far stronger or weaker than in previous years. On Monday, the House will begin action on the issue.

For many lawmakers, it is largely a question of whom they least wish to alienate: highly motivated and perhaps overly optimistic members of patient groups who believe that stem cells may soon save their lives or the lives of their loved ones, or equally passionate antiabortion activists who believe it is unethical to experiment on embryonic and fetal tissues.

But for the many publicly funded scientists who want to investigate the cells, the

Washington Post p. A8
Saturday Oct 9, 1999

Questions of Ethics, Efficacy Com

STEM CELLS, From A1

issue is a no-brainer: The nation ought to enlist their help, they say, because it is becoming increasingly clear that it will not be easy to turn stem cells into cures.

Among the more frustrating problems is how to get the cells to grow into the specific kinds of cells needed by patients, such as heart cells to be given to a heart attack victim or pancreas cells to be given to a diabetic. Today the cells behave as though they have a mind of their own, becoming whatever kind of cell they choose, and for no apparent reason.

"You smile at them and they become heart, you frown and they become brain," complained Tom Okarma, president and chief executive officer of Geron Corp. of Menlo Park, Calif., which has funded most of the human embryonic stem-cell work in this country. The challenges ahead, he said, "are formidable."

Indeed, while Okarma and others still hold high hopes that stem cells will lead to medical breakthroughs, ongoing studies by privately funded scientists at Geron and elsewhere have lent an air of sobriety to a field that a year ago seemed almost drunk with promise.

For example, it is still difficult to keep stem cells alive in the laboratory, and it has been impossible to grow them in

numbers large enough to be medically useful. Moreover, scientists still don't know how to engineer the cells so they won't be rejected by patients.

"The only way we're going to figure all this out is to roll up our sleeves and do the nitty-gritty research," said Harvard University cell biologist Evan Snyder. "There's such a clamor in the stem-cell field, but we should not let the clamor or the substantial promise seduce us into thinking we can do this quickly."

Embryonic stem cells are the basic, "plain vanilla" cells present at the core of newly developing animals. During prenatal development, they differentiate into more specialized cells, such as those that form the skin, liver, kidneys and brain.

What makes them unique is their ability to multiply indefinitely in laboratory dishes; where they can give rise to offspring cells that also have the ability either to blandly reproduce or, under the right influence, specialize into any of the body's tissue types. Doctors hope they will be able to grow a smorgasbord of replacement tissues from stem cells, for transplantation into people who need them.

After years of funding from Geron, two research teams announced simultaneously last fall that they had finally isolated human embryonic stem cells. One team retrieved them from young human embryos and the other from the immature sex organs of aborted fetuses.

The best news so far is that the cells seem to be as immortal as advertised, said James Thomson, the University of Wisconsin researcher who isolated human stem cells from leftover fertility clinic embryos. After almost two years of living and dividing in laboratory dishes, every new generation of cells seems just as young and full of potential as the previous one.

To prove that, Thomson has injected into mice freshly grown human stem cells that are more than 300 generations removed from the parent cells he isolated from his original human embryo. Stem cells that have retained their full potential should, when they are injected into mice, differentiate into all the many kinds of tissues that they can become. And these 300th-generation cells have done so with exquisite creativity, Thomson said, with some of them becoming hair, others teeth, and still others little masses of cardiac cells that soon begin to beat in unison like a miniature heart.

In fact, it is not difficult to get stem cells to differentiate into various tissues. The hard part is growing them into the specific kind of tissue you want—and keeping them from specializing until you are ready. Scientists will have to grow huge vats of stem cells in their undifferentiated state if they are ever to commercialize them. Currently, however, the only way to keep the cells in this "primordial" state is to grow them in small dishes along with a special type of mouse cell.

The mouse cells—known as "feeder cells"—somehow keep human stem cells from spontaneously following their urge to specialize. But despite valiant efforts, Thomson and others have failed to identify how the feeder cells do

THE NEW BIOLOGY

Human cloning, once thought impossible, today seems possible, and perhaps even probable. Growing spare body parts in the laboratory,

once the stuff of science fiction, is being pursued by scientists everywhere. Embryos are being genetically selected to be healthy, or male; "designer babies" may not be far behind. Plants genetically engineered to produce their own pesticides, and even certain types of plastics, are growing in fields. Science is en-

tering a new world where the once-unthinkable is suddenly doable. The Washington Post is examining this scientific revolution in a series of occasional articles about the new biology exploding at the turn of the century.



uplicate Hill Debate on Stem Cells

that. It is a bottleneck scientists will need to get through if the research is ever going to become useful for patients, because the mouse-cell system is too cumbersome to scale up to commercial levels.

It's not an impossible task. Several years ago, researchers working with mouse embryonic stem cells were in the same bind: Those cells only retained their full potential when grown with finicky feeder cells. Then researchers found that a compound secreted by the feeder cells, called leukocyte inhibitory factor, or LIF, was the magic substance that was keeping the stem cells vital. Since then, scientists have just had to add some LIF to their dishes of stem cells, eliminating the need for feeder cells.

"After that, the mouse studies took off," recalled Roger Pederson, a Geron-supported researcher of human stem cells at the University of California at San Francisco. Unfortunately, LIF does not do for human stem cells what it does for mouse stem cells, Pederson said. "Someone has to discover the LIF counterpart for human stem cells."

Perhaps even more daunting is the task of learning how

to prod batches of stem cells to mature into specific kinds of cells for transplantation into people, such as liver cells for patients with cirrhosis or specific kinds of brain cells for patients with Alzheimer's or Parkinson's disease.

Scientists have had some small successes in encouraging stem cells to turn into desired types, such as blood cells and nerve cells.

Last December, for example, Johns Hopkins University researcher John Gearhart stood before a Senate subcommittee and unveiled a poster-size photograph of spidery living cells with branched, outreaching arms. These appear to be healthy human brain cells, said Gearhart, grown in a laboratory dish from a starter batch of stem cells by feeding them a special recipe of nutrients. He plans to inject some into the brains of rodents this fall, to start assessing their potential as a treatment for brain diseases.

But Gearhart's method is far from foolproof. Many

See STEM CELLS, A9, Col. 1

STORE CLOSING ORIENTAL RUG SALE

FINAL 2 WEEKS

NO
REASONABLE
OFFER
REFUSED

Example:

Design	Size	Sale Price	Closing Price
Kashan	10x14	\$8970	\$2650
Bokhara	9x12	\$3590	\$1249
Chinese	10x14	\$5990	\$1500
Pak Persian	9x12	\$9890	\$3549

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Stem Cells Frustrate Scientists, Politicians

STEM CELLS, From A8

stem cells treated with the same nutrients do not become neurons, and retain the potential to become bone, muscle or other cells later on—cells that would not be welcome in a patient's brain.

Even less is known about how to spur stem cells to grow with assuredness into other kinds of cells, such as the insulin-secreting pancreas cells that, given the prevalence of diabetes in this country, are foreseen by Geron as the first "blockbuster" moneymakers. Somehow, researchers will have to overcome stem cells' apparently fickle.

Finally, there is the problem of immune-system rejection. Researchers want to figure out which molecules on stem cells are recognized as foreign by a patient's immune system. In theory, researchers could genetically engineer the cells to lack those molecules—a simple-sounding strategy that scientists concede will probably take many years to implement.

Depending on who is talking, problems such as these add up to an argument either for, or against, a quick infusion of federal funds.

To some on Capitol Hill, including Sen. Arlen Specter (R-Pa.), the many difficulties scientists face suggest that federal funds are needed if cures are to be developed within the next decade. Federal funding also would ensure a level of public oversight not possible when research is left to private concerns.

But others, including Rep. Jay Dickey (R-Ark.), say that given the vast number of unanswered questions in the field, the government could satisfy itself by funding basic studies on animals and less controversial human cells, without venturing into the ethical minefield of embryo research.

Further complicating the political problem, preliminary evidence from mice suggests that stem cells retrieved from embryos may have medical advantages over those isolated from aborted fetuses. That revelation, described in the Oct. 1 issue of the journal *Science*, is problematic for legislators such as Dickey. Last week, he sought to reword

the ban in a way that would have precluded research on embryo cells while allowing studies on aborted fetuses. Fetal research is less controversial than embryo research, because the former can be done on fetuses already aborted but the latter involves the direct destruction of embryos. Dickey later withdrew the proposal.

In the end, Congress may manage to duck the issue. During the past few months, the National Institutes of Health has created a set of guidelines and ethical standards that publicly funded scientists wishing to study human embryonic stem cells would have to follow.

The guidelines would preclude researchers from retrieving stem cells from embryos directly, because that act causes the destruction of live embryos. But researchers would be allowed to study stem cells from embryos that someone else had destroyed or from aborted human fetuses.

Many in Congress see the guidelines as a good compromise—and as a way to eliminate at least one controversial element from a bill that is already making waves with provisions relating to abortion and birth control. On Thursday, the Senate passed its version of the HHS bill with no restrictions on stem-cell research.

On Monday, the House will take up its version of the bill. And if representatives decide they can live with the NIH guidelines—a far from foregone conclusion—they too may drop the ban.

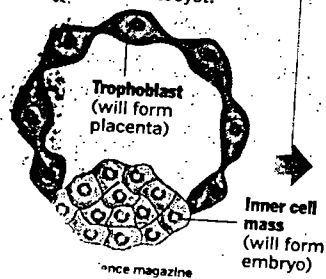
But the suspense might not end there. Many Congress-watchers predict that the House and Senate versions will defy congressional consensus on other counts, and ultimately will get folded into a huge omnibus spending bill.

Omnibus spending bills are negotiated outside the usual committee circles and are famed for ending up with unexpected changes—the result of horse-trading efforts in the wee hours of an already extended budget process. That means that, for all the lobbying on both sides of the issue, the legislative resolution to this year's biggest biomedical controversy may not become clear until the dust settles at the end of a frantic, closed-door session.

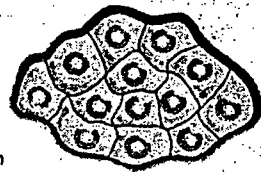
Growing Cells From Scratch

Scientists envision using stem cells from embryos or fetuses to grow human components such as heart muscle, bone marrow and brain tissue. Here is one approach, starting with a young embryo.

1. A 5-day-old human embryo, or "blastocyst."



2. Isolate the inner cell mass, which contains embryonic stem cells, each of which has the potential to grow into any kind of tissue.



3. Culture the embryonic stem cells in special broth to make colonies of cells, each destined to grow into a different kind of tissue.



4. Separate subpopulations of cells.



Kidney cells

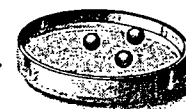


Bone marrow cells

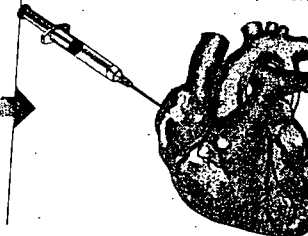


Heart muscle cells

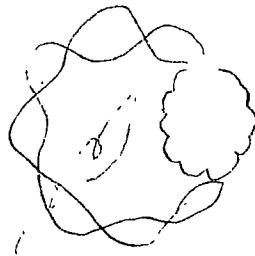
5. Engineer the cells so they are an immunological match with the patient.



6. For a heart-attack patient, inject heart muscle cells into the ailing organ, where they can integrate into existing muscle and perform work.



BY JOHN ANDERSON—THE WASHINGTON POST



5:45 6:15pm

WIFE → work

Green Room →

By 6:30pm

6pm - just
beginning

6-7 45pm

Magnet Mark?
Anal Mark?

