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What new millennium may bring

At the start of a new millennium, experts offer a glimpse of what scientific advances await us.

In recent decades, science has made huge strides, increasing human possibilities and extending man's reach with undreamed-of inventions.

For the new millennium, we asked top doctors and researchers from around the region for predictions in their fields.

Male pregnancy

"We're less than five years away from male pregnancy."

So predicts **Glenn McGee**, a bioethicist who specializes in reproductive issues at Penn's medical school.

A London scientist, he said, is convinced he'll be able to use a man's abdominal cavity as a substitute womb.

"You'd be surprised how many guys would want to be pregnant," McGee said.



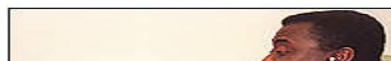
Glenn McGee



Kostas Daniilidis



Donald Dafoe



Mario Lemieux
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He also expects that within about two years, a human clone will be born, probably out of a scientific lab in Asia.

Designer babies will also become routine - with eager parents ordering up not just a boy or a girl but such traits as physical prowess and intelligence.

" 'Having babies' is as old as the stork," McGee said. "The new world is about 'making children.' "

He's certain that "this is definitely going to be the century for the strange." Already, McGee said, we've seen a 63-year-old mom, a designer IVF baby, \$50,000 eggs for sale, sperm Web sites, and a baby born from sperm harvested from a dead man.

"These sort of 'yuck' stories for today are already becoming normal for the next generation," he says. "We're going to spend the next 20 years figuring out the new social arrangements for love, sex and family."

- Susan FitzGerald

Virtual conferencing

Forget video conferencing. The next thing could be tele-immersion - sort of a hologram transmitted by phone.

Kostas Danilidis predicts tele-immersion will allow you to look toward a 3-by-5-foot screen and see a three-dimensional live image of another human being. When you

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- or your virtual conference partner - move, your perspective will shift, too.

"You really feel as if you're sharing a table with another person," Daniilidis says. You can look around to the side and you'll see the person's ear.

This is a technology of the near future. Daniilidis, a computer scientist at the University of Pennsylvania, and colleagues at four other institutions have already built a prototype, though he warns that it still suffers from a kind of video "noise" that looks like confetti fluttering through the air.

But once the bugs are worked out, the technology could allow far more than conferences. People in far-flung cities could build things together, codesign a building, perhaps, or a new automobile (though if it works the world should need fewer cars). Expert surgeons could be brought into virtual consultations in emergency surgeries, distant paleontologists could examine a new dinosaur skeleton, American children could experience African safaris from afar, cute robots with names like R2-D2 could display messages from princesses in distress.

We won't get into the possibilities of adult entertainment.

Daniilidis sees the technology first working its way into business settings and hotels. The Internet will need more bandwidth before it could be practical for private homes or schools.

Will people need to be concerned about their hair, clothes or makeup before answering the phone? "You can alter your virtual image," says Daniilidis, so, eventually, you may be able to add a virtual tie, or erase all your wrinkles and take off 20 pounds.

As enthusiastic as he is about the technology, however, Daniilidis says it won't be realistic enough to replace person-to-person contact. For one thing, you can't touch people - virtual feeling is still far down the road.

Photos by Jonathan Wilson, Inquirer Staff. During courtesy of Thomas Jefferson University, Daniilidis courtesy of University of Pennsylvania.

"Even with a perfect technical presentation, there will be some emotional thing which will be missing," he says. "Human contact will never disappear."

- Faye Flam

New organs

Donald Dafoe sees a day when patients who now wait for months, or even die waiting for an organ, will have far more choices.

Life will be better after transplant, too, says the chairman of Jefferson's department of surgery, because patients won't have to spend the rest of their lives being bombarded with chemicals that thwart the body from rejecting their new organ.

Within one to two decades, he predicts, scientists will figure out how to trick the immune system into accepting transplanted organs, freeing patients from immune-suppressing drugs. "There are some protocols in primates that work now," he says.

Xenotransplantation - transplanting organs from one species to another - could greatly increase the organ pool for humans within about the same time period. In the past, researchers would measure the success of a pig heart transplanted into a monkey with a stop watch, Dafoe says. Now, he says, he knows of a pig heart that has worked in a monkey for nine months.

Mechanical devices to replace or assist ailing hearts are also

improving rapidly, Dafoe says.

In the more distant future, scientists will learn how to prod stem cells into producing new organs. "That's an area that's really in its infancy," he says.

And, they're learning how to "build" organs and bone out of cells grown in the laboratory.

In the long run, Dafoe says, the only thing limiting our ability to replace worn-out parts will be money. How much will we be willing to spend to keep old people going?

- Stacey Burling

The racial divide

"In general," says **Kwaku Ohene-Frempong**, "the United States is moving in the direction where racial definitions are getting blurry."

From Ohene-Frempong's medical perspective, that means significant progress will be made in the next 20 years in closing the health-care disparity gap that today means African Americans are more likely than whites to die of heart disease, diabetes and AIDS.

As more blacks assume leadership roles in health care, says Ohene-Frempong, director of the Comprehensive Sickle Cell Center at Children's Hospital, they will be better positioned to fight diseases that take a toll on their population. He has been encouraged by the growing ranks of African American medical professionals who have dedicated their careers to fighting sickle-cell disease - an inherited blood disorder found mostly in people of African descent.

At major sickle-cell medical meetings, the attendance is largely made up of African Americans. By comparison, he says, Americans of European heritage make up the bulk of attendees at gatherings on cystic fibrosis - a hereditary disease that mainly afflicts whites.

"What you are seeing is people who feel close to a problem, trying to address it," Ohene-Frempong says. "You could also interpret that if people are not close to the problem, it will not be solved. That may sound bad, but I am not disturbed. People should come to work with passion. It is more likely that if you have a cousin or child with the condition, you will bring passion to the work."

While the race-based disparities in medical care should narrow, Ohene-Frempong voices no such optimism for another endemic

problem: Patients without money or health insurance will still struggle to get the care they need.

"Within each group, those who are poor will be those who are left behind," he says. "It is only when the U.S. adopts universal health insurance that poor and under-insured people can expect to receive adequate health care."

- Marian Uhlman

Gene therapies

Despite a sobering year for gene therapy following the September 1999 death of Jesse Gelsinger in a clinical therapy trial, **Katherine A. High**, a hematologist at Children's Hospital of Philadelphia, is optimistic about the future.

"The possibilities for gene therapy are enormous," High says. "It's basically a powerful technique. But it's not as straightforward as we once thought."

A leading gene therapy researcher, High predicts that some time this year, the country will see the first licensed gene-therapy products - likely gene-based drugs injected into cancer cells to treat head and neck tumors as well as melanoma.

The agents, which are being developed by biotech firms, could be used as powerful adjuncts to traditional chemotherapy and radiation, she says.

While conventional medicine aims to treat disease, gene therapy aims to cure it by replacing a defective or missing gene with a normal copy of the gene.

Over the last decade, the field wrestled with daunting technical challenges - how to get enough gene medicine into cells, how to keep it there and how to make sure the new genes, once they were delivered, got "turned on" so they could carry out their work in directing the body to produce certain proteins.

Now, however, progress is being made on all those fronts, High says.

Last year, she points out, French scientists used a form of gene therapy to restore the natural defenses of children suffering from an immune-system disorder that left them prey to life-threatening illness. It was the first clear success in a decade of gene-therapy research and American researchers are now gearing up to reproduce the

findings in small human trials.

People suffering from hemophilia could be the next to benefit, High says.

Her own work on a gene-drug for hemophilia B, in which people lack a blood-clotting protein known as Factor VIII, has shown promising results in preliminary safety trials. Three of six people taking the gene drug were able to reduce their daily reliance on injections with the blood factor.

High is now working on improved techniques in the hope that hemophilia B sufferers will be able to make enough of their own clotting factor to become free of injections with the artificial one.

This year, several other teams are expected to begin human trials of gene products to treat both hemophilia B and hemophilia A, the most common form of the disease.

Looking a few more years further, High foresees human gene therapy trials for Parkinson's disease; mucopolysaccharidoses, an inborn error of metabolism; and various forms of inherited blindness.

In the long term, High says, look for gene-therapy to combat cystic fibrosis, muscular dystrophy and perhaps even the loss of muscle mass that occurs with aging. "In a society like ours, with a rapidly growing older population, the potential importance of this would be enormous," High says.

- Huntly Collins

A warmer planet

The world will be warmer in the next 100 years - that's for sure, says **Eric Barron**, geophysicist and atmospheric modeler, Pennsylvania State University.

But how much hotter it will be and what that will mean to life on the planet remains the big question and "a major issue of research and debate in the coming century," Barron says.

"The evidence is pretty clear now that there has been warming and that appears to be the trend," says Barron, director of Pennsylvania State University's Earth and Minerals Environment Institute. "The real question we now face is understanding what that will mean for weather, agriculture, forests, cities."

The consensus of the scientific community is that by the end of the

century, average global temperatures will have crept up 2 to 5 degrees Fahrenheit.

"There is less uncertainty about the prospect of an increase than what its effects will be," Barron says.

To answer that question will require more collaboration among scientific disciplines - such as ecology, climatology, oceanography, atmospheric chemistry.

"It is going to take a multidisciplinary approach to figure out the effect of climate change on crops or forests," Barron says.

While the climate models have been "pretty successful" in depicting both historic climate variations and projecting future changes, he says, "there are still big areas that we don't understand."

- Mark Jaffe

The brain

Matt During has devoted much of his career to some of the most intractable brain diseases known - stroke, epilepsy, ALS, as well as a fatal childhood genetic disorder called Canavan's disease.

Progress is slow, patients are still dying, but During is excited about the progress that should come from science's new understanding of the role of genetics.

Genes influence people's predisposition to cancers, neurologic disorders, heart disease, diabetes and dozens more of today's biggest killers.

"The molecular biology and genomics revolutions are changing the way we think about diseases," says During, director of Jefferson's Central Nervous System Gene Therapy Center. "We'll be able to profile people based on gene chip analysis" - a reference to the idea that one day soon you'll be able to carry a profile of your individual genetic code on a silicon chip.

Rather than the one-size-fits-all approach of the past, medicine would be customized to work with specific genetic types. "Everyone responds differently to different drugs," During says. Doctors may soon prescribe medicines tailored to suit patients' genetic profiles "instead of poisoning people with drugs that have no benefit to them."

In During's field of neuroscience, doctors will become more attuned

to the physical, chemical and genetic roots of psychological disorders.

It used to be that "functional disorders" such as depression, learning problems, eating disorders or drug addiction were the purview of psychiatrists, while neurologists dealt with physical illness.

"That's the way I was taught," he says, but now "that's completely gone."

Not that the therapist's couch is likely to go the way of the horse and buggy. There's growing evidence that talk therapy can change the physical and chemical makeup of the brain, just as a traumatic incident can.

Still, advances in genetics could open up a whole new world of drug treatments - and then help doctors better determine which patients would benefit from pills rather than words.

- Faye Flam

Longer life

Joel Posner foresees that sometime in this new century, human beings could begin living extra hundreds of years - or more.

Really.

Hugely extended life spans will be the result of scientists' current work allowing human cells to keep dividing, cancer-free.

Currently, cells can divide only a certain number of times before they die - and the person dies. But by adding a small piece of protective DNA - called telomerase - to human cell cultures, scientists appear to keep those cultures dividing "forever," Posner says.

"The technology is not so far away that someone can modify the human chromosome so that the . . . maximum life span may be expanded almost limitlessly," predicted Posner, who holds the Audrey Meyer Mars Chair of gerontologic research at Medical College of Pennsylvania-Hahnemann University.

Even if people don't start living so long that they enjoy their great-great-great-great-grandchildren, regular "tune-ups" will help extend their life spans.

Like cars that regularly go in for service, men and women will visit

wellness centers and local hospital aging centers to get checked for indicators of aging: vascular dysfunction, fat accumulation, insulin resistance, and loss of muscle.

Posner currently runs such a center in Philadelphia, funded mainly by a grant from the National Institutes of Health. He says about 400 people over 60 attend regularly and learn ways to slow the aging process, including exercise and new diets.

With so many people living longer, society will face the next challenge.

"There are six billion people alive now," he says. "Suppose nobody dies?"

- Loretta Tofani

Early warnings

Go for a physical 100 years from now and a routine brain scan may detect early signs of Parkinson's, Alzheimer's and other devastating neurological ailments.

Much like Pap smears and mammograms today, the brain scans of the late 21st century will serve as an early warning system, says Hubert Schoemaker, who in 1979 cofounded the region's trailblazing biotechnology company Centocor Inc. Doctors will be able to arrest neurological disease by injecting healthy cells into the brain in what will be seen as basic preventive medicine, says the MIT-trained biochemist.

"We will figure out how the brain works, how we store memory and how we process things," says Schoemaker, who founded Neuronix Inc. of Malvern in 1999 to develop new biotech drugs. That knowledge will translate into treatments for diseases that now slowly rob people of their ability to think, speak or move.

Already, Schoemaker says, companies are developing new generations of CAT scans and MRIs which provide images that were impossible to capture just three years ago. While neuronal cell replacement is an idea still in its infancy, academic institutions and companies such as Neuronix are exploring such a possibility.

"The 21st century will be the century for the brain and brain-related disorders," Schoemaker says.

- Marian Uhlman

The cosmos

As if it weren't enough that the pace of life and the growth of information seem to be accelerating, now it appears that the universe itself is accelerating - that is, intergalactic space is stretching faster and faster, carrying galaxies farther and farther apart.

That may not be a major concern for most of us - Earth and the other planets are held firmly in orbit around the sun by gravity. But for Paul Steinhardt, it's a tantalizing mystery.

And it's one whose solution promises some completely new picture of the universe to emerge in the coming decade or so.

To drive the acceleration of the cosmos, something must be exerting a kind of outward force. It may be a constant of nature - what physicists call a "cosmological constant." Or it could be a kind of "dark energy" that pervades the universe. In Steinhardt's version of the theory, it is called the "quintessence," named after the mysterious fifth element proposed by the ancient Greeks, following air, earth, fire and water.

Astronomers started to come to terms with cosmic acceleration in just the last couple of years. They were still contemplating some other unsolved puzzles, including what appears to be a preponderance of invisible material dubbed "dark matter," whose nature also remains to be discovered.

(Astronomers have taken to using the term "dark" to describe anything they suspect exists but can't find.)

Steinhardt is working on that problem, too - he has a new theory describing a particular brand of dark matter that he calls "self-interacting." He and others suspect that the dark matter helped shape the visible matter into stars and galaxies. But the universe seems to be full of mysterious "dark" elements.

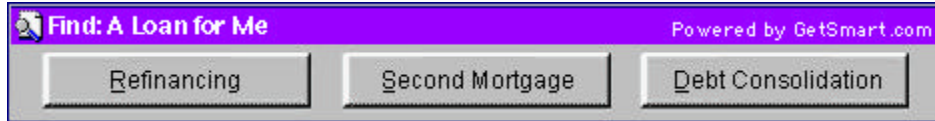
Steinhardt expects astronomers to make great progress in understanding our strange universe in the coming decade, thanks to a wealth of new kinds of observations.

"A number of technologies - adaptive optics, X-ray satellites and microwave detectors all began to mature at the same time," he says, describing some of the new ways scientists are studying the heavens.

Will these new technologies help scientists to eventually figure out the answers?

"That assumes there are a finite number of fixed questions,"
Steinhardt says. More likely, he says, "We'll have new mysteries."

- Faye Flam



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