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COMING //

- **JANUARY:** *Simulation in Healthcare*, the first journal dedicated to the subject, will put out a preview issue (regular quarterly publication begins in March). Published for the Society for Medical Simulation, it will focus on clinical research results, simulation techniques and technologies, and commentary on the field.
- **FEBRUARY:** The European Union will release a report on an avian flu simulation exercise across all 25 member states, Norway and Switzerland. In one of the largest such operations ever attempted, the countries enacted a worst-case flu pandemic scenario in November to examine communication and preparedness plans across borders.



FOCUS // **POLIO HAS RESURFACED** in central Minnesota, 27 years after the last case in the United States was seen. Officials are trying to piece together how an eight-month-old Amish girl and four other children acquired the virus this past fall. Dr. Susan Rutten (shown making a house call) thinks the Amish, who often choose not to get vaccinated, have acquired the infectious disease either from traveling outside the United States or from contact with a foreign visitor. "If polio is in this community," says Rutten, "I guarantee it's in other parts of the country."



INTERVIEW //

Before the Fall

■ BY ALICE PARK

On Thanksgiving Day, when Korean stem-cell pioneer Woo Suk Hwang admitted that an associate had, without Hwang's knowledge, purchased human eggs, and that he himself had lied about egg donations that junior members of his research team had made to his study, the announcement made headlines around the globe. Not that media attention was anything new for the researcher, whose laboratory at Seoul National University had been credited with a list of firsts: the first stem-cell line derived from a mature human cell; the first lines from the mature cells of diseased patients (a

step toward helping patients grow their own replacement tissue); and the first cloned dog.

But Hwang's ethical lapse turned out to be only the tip of the iceberg. After investigating charges by Hwang's fellow researchers, a team at Seoul National University confirmed that some data in the experiments involving diseased patients' stem cells had been fabricated. Hwang has resigned, but stands by his claim that he has discovered how to produce stem cells that genetically match those of patients. Investigators are looking into this claim and his other work.

Our interview preceded the controversy, but it opens a window onto Hwang's methods, motivation and relationships with his lab "family," perhaps explaining, in part, recent events.

Q: Do your advances bring us closer to cloning humans?

A: I believe cloning humans would be very difficult and very unsafe.

Q: So why did you choose to pursue stem-cell research?

A: My father passed away when I was five years old, and our mother supported six children by raising cows. She said to me: "Please become a great scientist rather than a rich businessman." Because I cared for cows when I was young, I decided to study them when I went to school. When I moved to a faculty position at Seoul National University in 1986, I made it my research goal to improve the reproductive efficiency of the elite animals that produced the highest quality and yield of milk and meat. I thought the best way to maintain this high yield was to clone them.

Q: President Bush has said he is worried about a world in which cloning becomes "acceptable."

What would you tell him about your work?

A: I have no comments on President Bush's statements, but I hope stem-cell researchers can do their research more freely soon. I am just a scientist, and I want to concentrate on science.

Q: What makes your approach unique?

A: We transfer the whole somatic cell instead of just the nucleus, which makes the process more efficient; it allows us

to obtain one stem-cell line from just 10 donated eggs. We've also devised special techniques, such as squeezing the recipient egg to remove its nucleus before inserting the somatic cell in order to minimize any damage to the cell. And we've developed unique cultures made up of only human cells to nourish the cloned cells. Since animal cells are not used, there is no contamination. And nonhuman cells may make it difficult for the cloned cells to grow.

Q: Your work style could almost be called tender.

A: I think all cells have a spirit; they know if someone is there. I ask my researchers to make sure one of them is always in the incubating room where

■ **“I think all cells have a spirit; they know if someone is there. I ask my researchers to make sure one of them is always in the incubating room where the stem cells are kept.”**

the stem cells are kept. For this kind of work, you need to insert some human spirit; you cannot only use machines.

Q: Your day in the lab is a long one.

A: I wake up at 4 a.m., and I come to the lab by six to check the stem cells under the microscope. Until 11 a.m., my research team extracts eggs from cow and pig ovaries; then they go to their own projects. We have a meeting every afternoon to discuss our progress, and three times a week we have

evening seminars with graduate students from the other schools at Seoul National University to discuss our work and theirs and to learn from each other. That lasts to 11 p.m. I usually go home around midnight.

Q: With all the time you and your research team spend together, are you a close-knit group?

A: They are like my children. Their generation has no time for dating, so half of them are lab couples. Once a week, we hike in the mountains; it's good for everyone to get out of the lab.

Q: How did you succeed in cloning a dog when many others have failed?

A: The difficulty is in obtaining the eggs. We were able to determine the exact ovulation and embryo-transfer times. Our team was ready to collect oocytes at any time of day, even midnight or early morning. Our long hours and work style helped indeed.

Q: Many South Koreans think you should win a Nobel Prize.

A: My goal is not to win a Nobel Prize but to improve human dignity and well-being. ■

BY THE NUMBERS //

Seniors at Risk

18.4 Average number of prescriptions filled by each Medicare enrollee in 1992 (including refills)

29.7 Average number of prescriptions filled by each Medicare enrollee in 2000 (including refills)

67 Percentage of nursing-home residents with adverse drug events over a four-year period

15 Percentage of those events that resulted in hospitalization

28 Percentage of elderly patients who, in one year-long study, filled prescriptions for a potentially problematic psychotropic drug

5 Percent chance that, in 2000–2001, an elderly HMO patient received a drug categorized by the widely used Beers criteria as “always avoid” because of general inefficacy or high risk of toxicity

1.9 Millions of adverse drug events (estimated), including allergic reactions and unintentional overdoses, in Medicare enrollees in 2003

180,000 Number that were life-threatening or fatal

475,000-plus Number that, with better prescribing and monitoring, might have been prevented

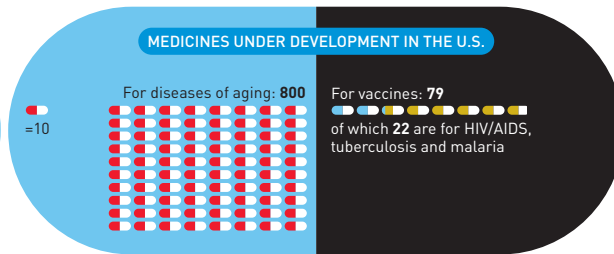
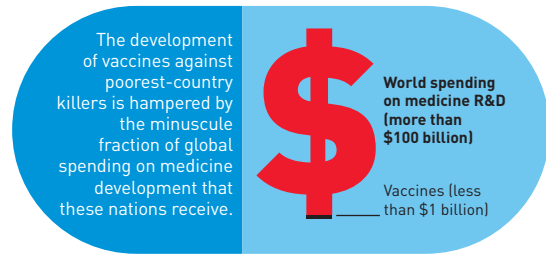
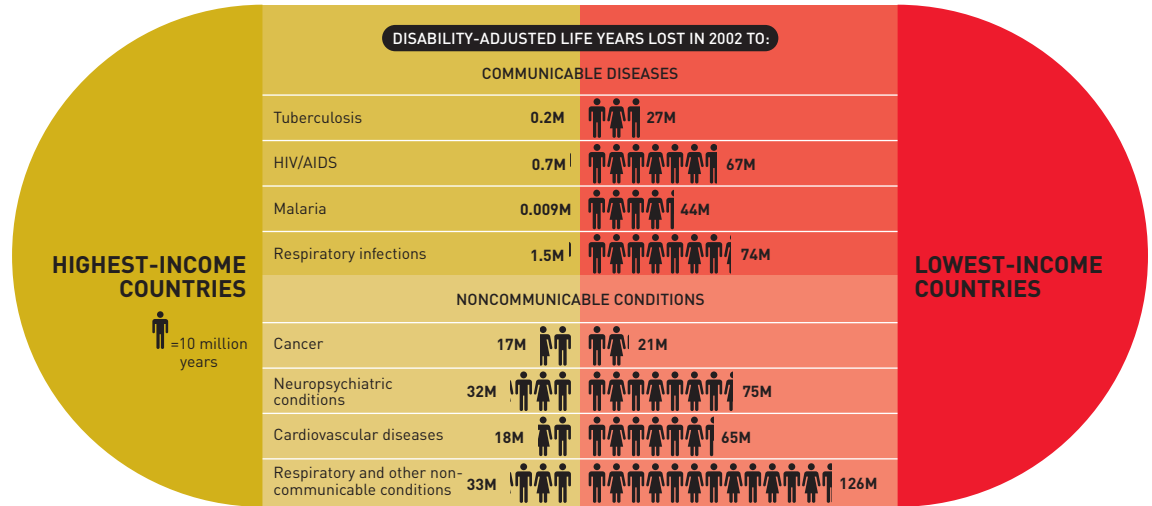
Making Markets for Vaccines

Nothing spurs innovation like the promise of profits, which motivates pharmaceutical companies to spend the hundreds of millions of dollars necessary to develop a single drug. As drugmakers devote their efforts to curing diseases of aging, for which there are lucrative markets in wealthy countries, the poorest countries are forgotten. Only 10% of global spending on drug development goes toward prevention and treatment for ailments that affect 90% of the world's population. Such brutal economics have hindered the search for vaccines against HIV/AIDS, malaria and tuberculosis, which each year kill approximately 5 million people.

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THE WORLD'S GREATEST KILLERS

Disability-adjusted life years (years lost to premature mortality and disability) tell the story: While communicable conditions take an awesome toll in the poorest countries, diseases of aging, including cancer and heart disease, are of greater concern in affluent countries.

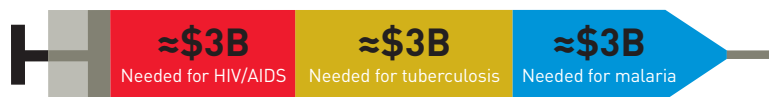
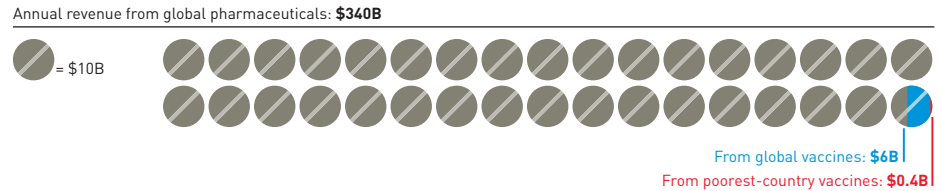


THE VACCINE DIVIDE

In terms of medicine R&D, the poorest countries are largely ignored.

THE BELEAGUERED BOTTOM LINE

For drug companies looking to develop vaccines for the poorest countries, the economics are bleak. There are simply few profits to be had.



MARKET FORCES TO THE RESCUE

In an approach called advance market commitments, rich countries would promise to pay for vaccine dosages on behalf of the poorest countries—providing to drug companies the incentive to devote R&D to poor-country diseases. G7 finance ministers have agreed to a pilot program based on a proposal by the Center for Global Development, a Washington, D.C., think tank that seeks commitments of approximately \$3 billion each for HIV/AIDS, tuberculosis and malaria.

SOURCES, FROM TOP: WORLD HEALTH ORGANIZATION; GLOBAL FORUM FOR HEALTH RESEARCH; PHARMA; CENTER FOR GLOBAL DEVELOPMENT

ADVANCES //

Slimmer Life-Span Gains

EATING LESS may prolong the lives of mice by 67%, but cutting calories may not similarly hyperextend human life, as some have theorized, say scientists from the University of California at Los Angeles and Irvine. After comparing the longevity of Japanese sumo wrestlers (who average 5,500 calories per day) with that of typical Japanese males (2,300 calories), the researchers hypothesized that restricting one's daily diet to even as few as 1,500 calories may prolong human life a mere 7%. In both mice and men, restricted caloric intake decreases fertility—a more pronounced effect in mice because they invest 10 times as much energy in reproduction. sciencedirect.com; search for “dietary restriction substantially”

TRACE AMOUNTS OF psychiatric, anti-epileptic and veterinary drugs, among other sorts, have turned up in drinking water from the most advanced water-treatment plants in the United States, the United Kingdom and Italy, British scientists say. These drugs enter the drinking-water supply via sewage-treatment plants that discharge “cleaned” water with traces of unmetabolized drugs into rivers and streams. Researchers say that the long-term effects of consuming a cocktail of prescription drugs (however low the dose) are unknown. But it could take a lifetime of drinking two liters of tainted water a day to ingest a single dose of a single drug.

sciencedirect.com; search for “drinking water human pharmaceuticals”



THE CLEANER SEX? It's women, according to a Harris Interactive survey of hand-washing habits. When asked if they always wash after using a public restroom, 94% of women polled said yes, compared with 88% of men. But when unknowingly observed in public restrooms across the country, only 90% of women washed, compared with 75% of men. Both sexes admit they are less likely to wash after using the facilities at home, where no one's watching. cleaning101.com/newsroom/2005_survey/handhygiene

SIGHING is a respiratory function meant to prevent the lung from collapsing, but according to Polish researchers, in social mammals (including humans) it may have evolved to communicate relief in addition to its respiratory role. To test this theory, they caged lab rats in individual chambers, gave them a series of shocks and conditioned

them to expect a respite after a safety signal. Sighs were 7.5 times more frequent during the relief period; variations in how they sighed proved that the sighs were intentional, not reflexive, perhaps meant as an all-clear signal, the scientists say.

sciencedirect.com; search for “rats sigh relief”

MICROGRAVITY TECHNOLOGY developed for NASA is being used to produce larger quantities of cord-blood-derived embryonic-like stem cells, or CBEs. Using spinning devices, researchers at the University of Newcastle suspend the cells in a liquid, which allows them to grow faster than if they were on the flat surface of a laboratory dish and also minimizes damage to the cells. In large amounts, CBEs could help reverse liver, brain and vascular tissue damage. ncbi.nlm.nih.gov/entrez/query.fcgi; search for “McGuckin”

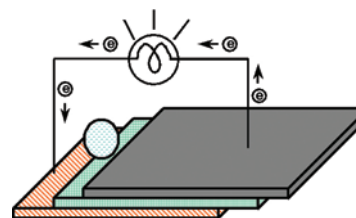
THE CUTTING EDGE //

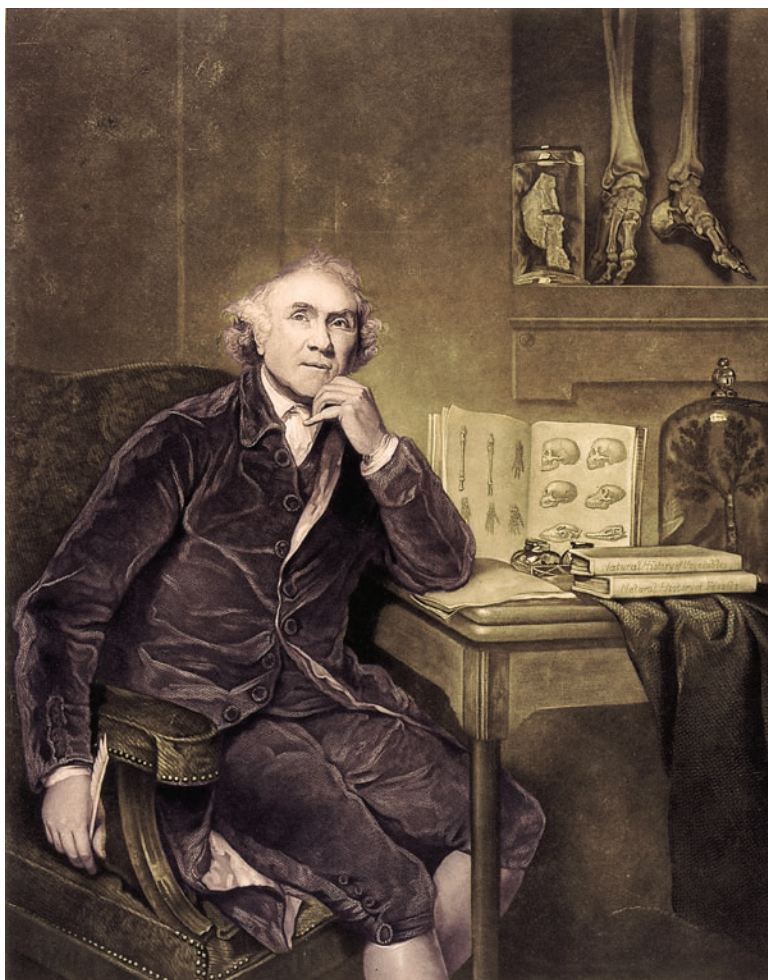
Pee Power

The next time you flush, consider the potential source of energy you're wasting.

Korean scientist Ki Bang Lee has developed a urine-fueled battery that can power home tests for kidney disease, blood-glucose levels and even some pregnancy abnormalities. The battery (diagrammed above) is the size of a credit card and made of paper soaked in copper chloride (middle layer) sandwiched between strips of magnesium (upper) and copper. It produces a small electric charge when urine reaches the copper (electricity is needed to run biosensors and display test results).

The paper battery could eventually be integrated into any small biochip system that tests urine for disease and could be modified to test saliva or blood samples. Scientists say it could even eventually activate any electric device with low energy consumption, such as MP3 players and cell phones.





EXCERPT //

A Most Curious Surgeon

In the world of Georgian England, where physicians didn't deign to touch patients and left surgery to the professionally inferior surgeons—or barbers—a Scot named John Hunter fed his insatiable appetite for anatomical information by carving up thousands of corpses (and so, incidentally, helped to spur a thriving body-snatching business). In The Knife Man: The Extraordinary Life and Times of John Hunter, Father of Modern Surgery, Wendy Moore escorts readers inside Hunter's classroom in his brother's Covent Garden anatomy school, where students were encouraged to rally all their senses for observation. It was a far cry from today's medical schools, which are starting to bring part of their anatomy lessons into the untainted virtual world.

Since the guts were the first parts to putrefy, the students would begin by slitting open the abdomen, folding back the flaps of skin and fat, and examining the organs of digestion: the stomach, the more than 30 feet of intestines and the smaller organs, such as the spleen, gallbladder and pancreas, packed tightly into the abdominal cavity. Next, they would open the chest, sawing apart the rib cage to expose and remove the lungs, the lobes of which were blackened by London's ubiquitous winter smogs; mastery of dissection demanded not only intricate skills with a knife but brute strength with a hacksaw. The lungs discarded, the pupils could examine the heart, which even the most novice anatomist now knew, having studied Harvey, to be the center of the human physiological system. Hunter would then help the pupils with the tricky task of inspecting the other main organs—the liver, bladder, kidneys, reproductive organs and brain—encouraging them to probe the cavities with their fingers, follow the vessels with their knives and weigh the organs in the palms of their hands. Finally, they could work on the muscles, which decayed slowest, and the

bones, which Hunter showed them how to wire together to create their own articulated skeletons.

Anatomy was invariably a sensory experience. As well as being subjected to the all-pervading odor of decay, the crackle of the dried membranes and the need for intense visual inspection, students were urged to feel the textures of the different parts and even to taste the body fluids.... Hunter frequently employed his sense of taste in dissection, and he encouraged his pupils to do likewise, as he recorded matter-of-factly: “The gastric juice is a fluid somewhat transparent and a little saltish or brackish to the taste.” And he once observed, “The semen would appear, both from the smell and taste, to be a mawkish kind of substance; but when held some time in the mouth, it produces a warmth similar to spices, which lasts some time.” ■

Half-Baked or Brilliant?

The expanding universe of bloggers—people who post personal commentary on the Internet—now includes a galaxy of medical professionals. Dozens of sites are being composed by physicians, nurses and hospital staffers who regularly rant on topics from public policy to the top 10 “Worst Intern Duties.” Here, passages from the blogs of three noteworthy practitioners.

Hospital Innovations That Do Not Exist...Yet

Adapted from an Oct. 21, 2005, posting on Intuери.org, a blog written by “Maria,” a resident physician in psychiatry

Instead of donning a gown and a pair of gloves for every patient who is on contact precautions, physicians and nurses would walk through an antimicrobial force field in the doorway of the patient’s room. It would be like a thin waterfall tumbling from the ceiling to the floor. People would automatically become “drenched” in this force field and protected against infectious diseases. And somehow, when the person walked out, the force field would be removed and the entire system would disinfect itself. Maybe with continuous magnetic or electric pulses. Or something...

More Thoughts on Supply and Demand

Adapted from an Oct. 25, 2005, posting by “rcentor” on Medrants.com, which sounds off on public policy and medical news

The concept of our reimbursement system is bankrupt. If you pay me for a unit of care, regardless of how much time I spend, I will look for ways to decrease the time of that unit of care. If I can see seven patients rather than six in two hours, I have increased my gross income by 17% without significantly changing my overhead! But I also had to decrease each patient visit by approximately three minutes.

Those three minutes matter! They allow the physician to ask a few more questions and answer a few more questions. They improve the doctor-patient relationship. Without three minutes, we may leave out something important from the visit.

Tips for the Emergency-Department Drug Seeker

Adapted from an Oct. 9, 2005, posting on Gruntdoc.com, a blog analyzing top medical stories daily, by “Allen,” a Texas emergency-medicine doctor and former Marine doc, also known as a “grunt” Tonight a patient reminded me there are limits to drug-seeking behavior in the emergency department (ED). I’d like to pass on some words of wisdom. Don’t:

- start screaming for another doctor 30 seconds after being told “no pain shot”
- ask the nurse, “Is taking seven Darvocet like taking one hydrocodone 7.5?”
- think “the only drug that works for me starts with a D...” isn’t going to make us less wary...
- ask, “Is Doctor X on duty?” (knowing the names of the ED docs is never a good sign)... ■

Birth of the Pill

The poor, mostly uneducated women who lined up in San Juan, Puerto Rico, 50 years ago didn’t know they were participating in the first large-scale clinical trial of a medication. But they did know the pill they’d been asked to try promised an amazing benefit: Taken properly, it would prevent pregnancy.

Soon to be known simply as the Pill, the first oral contraceptive was developed by Gregory Pincus, an endocrinologist, and John Rock, a gynecologist. But the idea had originated almost four decades earlier, the brainchild of birth-control activist Margaret Sanger.

By the time Sanger met Pincus in 1951, scientists had discovered the role of progesterone in repressing ovulation in pregnant women. When she persuaded him to pursue a birth-control drug, he imagined a pill that would mimic progesterone’s effect in women who weren’t pregnant.

By 1953, Pincus and Rock had settled upon progestin, a synthetic version of progesterone, as the Pill’s active ingredient. A small trial proved the drug’s effectiveness, but finding a site to conduct the large-scale trials necessary for regulatory approval was another matter. Thirty states had nineteenth-century laws banning even dissemination of birth-control information. But in Puerto Rico—struggling with poverty and rapid population growth—officials welcomed the trials.

Seventeen percent of participants, taking pills

that contained much higher doses of hormones than are used today, reported nausea, headaches and other discomforts. Pincus and Rock concluded that these symptoms were largely psychosomatic. More notably, not one participant became pregnant. The Food and Drug Administration (FDA) approved a formulation, Enovid, in 1960, and within two years a million women were taking it.

Contraceptive formulations now contain lower hormone levels that minimize the



risk of heart attacks. But more revolutionary changes are in store, says Regine Sitruk-Ware, a reproductive endocrinologist at the Population Council in New York City. Researchers are developing molecules that prevent conception by tweaking an enzyme in sperm cells so they won’t bond to eggs. Such methods are 15 to 20 years from the market, says Sitruk-Ware, but within five to seven years the FDA could approve a male contraceptive that suppresses sperm production. ■