Injecting stem cells gives damaged hearts the bypass surgery (who received stem cells pumped blood more to replenish blood flow. Vessels are transplanted into the damaged area—from the bone marrow. Scientists at the University of Pittsburgh have begun a trial with a new twist that they say will help settle the debate. The researchers are injecting stem cells into the hearts of individuals set for a heart transplant and then examining the removed hearts to see how the stem cells behave.

Based on preliminary evidence, the researchers say, the stem cells appear to fuse with heart cells and give them a much-needed boost of fresh mitochondria—but the idea has already met with skepticism. Heart tissues that are starved of oxygen, either chronically or from a heart attack, are unable to pump blood efficiently, forcing the remaining muscle to try to compensate by pumping harder. Eventually, that stress leads to heart failure. Because the heart has a limited capacity to heal itself, the only option for these individuals was to have a transplant—until the stem cell therapy.

Studies had previously shown that injecting stem cells into mice that had suffered artificially induced heart attacks improved how the heart muscles contract. But some researchers warned that moving into human trials without understanding the exact effect of injecting stem cells was risky and premature (Nat. Med. 10, 445–446; 2004).

Since then, however, clinical studies have begun to show that injecting stem cells derived from the bone marrow can help heal damaged hearts. For instance, in one trial in Argentina, researchers injected 10 individuals who had suffered heart failure with stem cells taken from their own bone marrow.

The stem cells were injected along with a coronary artery bypass—into which healthy blood vessels are transplanted into the damaged area—to replenish blood flow. Six months later, those who received stem cells pumped blood more efficiently than the control group, who only had the bypass surgery (J. Thoracic Cardiovasc. Surg. 130, 1631–1638; 2005).

Researchers at the University of Rostock in Germany have found similar results in their study of 55 individuals. They are set to report their findings at the American Association of Thoracic Surgery in May. Mexican researchers last year also reported encouraging results from their trial in five individuals (Life Sci. 78, 279–283; 2006).

But scientists continue to question the mechanism behind the effect: do the stem cells transform into heart muscle? Do they merely fuse with the heart cells? Or does injecting stem cells stimulate the release of compounds that help the heart recover from damage?

Some researchers say it’s extremely unlikely that the hematopoietic stem cells, which normally give rise to blood cells, would ‘transdifferentiate’ into a completely different cell type, such as a myocyte—a heart muscle cell.

But others, including Piero Anversa, director of New York Medical College’s Cardiovascular Research Institute, maintain that this is precisely what happens. “I believe our data have shown unequivocally that [the cells] have the properties to transdifferentiate into cardiomyocytes and coronary vessels,” Anversa says.

The answers may be forthcoming from the new trials.

Doctors will inject stem cells into only one-half of the left ventricle of individuals slated for a heart transplant. The other half of the left ventricle gets a placebo saline injection. The idea is that, following the transplant, the removed heart would reveal the fate of the stem cells.

The trial began in February and as of mid-April, the researchers had data from three hearts. Their preliminary findings suggest that the stem cells are fusing with the host’s ailing heart cells, creating a larger number of binucleated cells in the injected area than in the control. “I know we don’t have true differentiation into a cardiac muscle,” says lead investigator Amit Patel, director of the Center for Cardiac Cell Therapy at the University of Pittsburgh.

Patel says the stem cells might help the heart by providing fresh mitochondria and allowing for stronger, synchronous contractions.

But he will need a lot more data to convince the skeptics.

“The notion of a mitochondrial donor would require a huge number of fusion events to have an impact on heart function,” says Loren Field, professor of medicine at Indiana University. At least in rodents, Field says “fusion is not a very prevalent event.”

Anversa doesn’t buy the fusion theory either. “It seems more reasonable to me that bone marrow cells differentiated into new myocytes and improved function, rather than old myocytes being modified by fusion to become better cells,” he says.

Although the procedure is still in trials in the US, it is already in practice elsewhere. For instance, Patel in December 2005 treated Hawaiian singer and entertainer Don Ho in Thailand. At 75, Ho was not a heart transplant candidate, but following the therapy has improved enough to perform on stage twice a week. Several centers in South America and in St. John, Barbados, also offer the treatment.

Patel says he wants to understand how the therapy helps people, but what really matters in the end is that it does. “If it works, whether it’s through a paracrine effect or fusion or true transdifferentiation, which is what everyone hopes for,” he says, “then that’s fine.”

George S. Mack, Columbia, South Carolina
Sheep study calls for closer look at prion hypothesis

The infectious agent behind diseases such as mad cow, scrapie and variant Creutzfeld-Jakob disease may not necessarily be rogue prion proteins, says British researchers—a suggestion that flies in the face of current dogma about how these diseases are spread.

Although deformed prions are a characteristic of these diseases, they may not be the initial infectious agent, says lead researcher Martin Jeffrey of the Veterinary Laboratories Agency—Lasswade near Edinburgh. The researchers are basing their theory on how these proteins are absorbed in the sheep gut.

Experts contacted by *Nature Medicine* declined to comment on the controversial paper.

The scientists inoculated sheep intestines with brain extracts containing the abnormal form of the prion protein (PrP), the hallmark of the killer neurodegenerative disease. But when they later examined the infected sheep, the rogue protein had congregated at entirely different sites (*J. Pathol.*, **209**, 4–14; 2006).

“Despite the fact that the Nobel Prize was awarded for the prion hypothesis, there remains the possibility that it’s not the correct explanation,” says Jeffrey. “There needs to be a more asiduous investigation of the causes of this group of diseases.”

The study also suggests that the mechanism of resistance against these diseases does not operate at the level of gut absorption, as some researchers had said. The 50 sheep studied displayed different levels of resistance to scrapie, but all absorbed the prions equally readily.

Although the study suggests that prion proteins can be absorbed by the gut, this seems to happen only rarely, at least in sheep. If the same is true of humans, then scientists may need to rethink exactly how the consumption of tainted meat leads to disease.

Security fears plague deadly disease lab’s move to central London

Plans to shift the UK’s leading medical research institute to central London are under fire because the move would include the institute’s facility for working with dangerous pathogens.

In July 2005, the Medical Research Council (MRC) announced a plan to relocate the prestigious National Institute for Medical Research (NIMR) from its home in suburban Mill Hill to London. The MRC has claimed that the move would foster more clinical research, primarily through collaboration with the University College London and its teaching hospital. The announcement came after months of acrimonious debate between the council and the institute’s researchers (*Nat. Med.*, **10**, 762; 2004).

British intelligence and local politicians are now raising doubts about the MRC’s plan to house the institute’s level-4 containment facility on the eleventh floor of a new building in the heavily populated area.

According to a report in *The Evening Standard*, the UK’s M15 National Security Advice Centre has raised “grave concerns” about the potential release of dangerous pathogens, either through a terrorist attack on the building or during transportation to and from the facility. M15 has to approve any plans for level-4 facilities.

Nick Winterton, the MRC’s executive director, downplays the security concerns, saying the initial proposal is “a fairly broad-brush feasibility plan.” The MRC is considering several options including separating the level-4 facility from the institute’s new location, he says.

But NIMR scientists say splitting the facility would seriously hamper research. “It would be grossly inefficient,” says Jonathan Stoye, head of the institute’s division of virology. Much of the research at the facility involves animals that must be monitored constantly, Stoye says. “You’d have people running backwards and forwards several times a day. I don’t think you can run a facility on such a basis.” An NIMR report last April strongly recommended including the lab in any relocation plans.

The facility—equivalent to a US biosafety level-4 lab—is one of only a handful in the UK and is being used almost exclusively for analyzing samples of flu virus from around the world. The lab is part of a World Health Organization network that works both on the H5N1 bird flu virus and more conventional strains included in each year’s flu vaccine. But its focus is expected to expand to include other emerging diseases.

Winterton says it may be possible to relocate the lab and still address security concerns. “Many hospitals and universities in London have high-level containment facilities,” he notes. The MRC may also consider other options, including using facilities already in the city or building a new lab on a separate site.

How easy it will be to move the lab may depend in large part on community response, says Edward Hammond, US director of the Sunshine Project, a nonprofit group that opposes biodefense research. Hammond notes that some facilities in the US have been stopped by local opposition, but openness may go a long way toward assuaging concerns. “Transparency must come above all,” he says.

A final proposal on the lab is expected by October, and construction on the new NIMR is slated to begin in 2009.

*Geoff Brumfiel, London*
Cell-based tests tackle predicting safety of antibody drugs

The disastrous trial in the UK in March clearly illustrated one thing: the tests we rely on to predict how a drug will behave in people are outdated. Scientists in Europe are developing new tests to help get a better picture.

In the UK trial, six men suffered severe immune reactions to an experimental leukemia drug. Tests in animals revealed nothing extraordinary, and the investigators ruled out any possibility of contamination in the drug.

There are many unresolved questions about that trial (Nature 440, 856; 2006), but the human body’s response to the drug, based on a monoclonal antibody, proved particularly unpredictable.

Up to 30% of experimental drugs fail in clinical trials. Because of differences in immune makeup, animal models are likely to be even poorer at predicting the toxicity of protein-based therapies.

“These types of drugs make up more than 50% of new drug applications,” notes Thomas Hartung, head of the European Centre for the Validation of Alternative Methods (ECVAM). “We can’t use toxicology that is 60 years old.”

In March, ECVAM approved six new toxicology screens based on cultures of human cells. Five of the tests detect pyrogenic contaminants in drugs—for instance, bacteria that can infiltrate injectable or intravenous drugs during manufacture and cause lethal immune reactions. The tests rely on cultured human white blood cells, and might replace two expensive current methods—the Limulus assay and testing on rabbits.

The new techniques improve on both methods. The Limulus assay picks up only a subset of bacteria, but these methods detect most bacteria, viruses and fungi. Drugs not suitable for the Limulus test, such as monoclonal antibodies and other biological compounds, are typically tested in rabbits. But the tests only provide a simple yes or no for contamination and cannot quantify the amount of toxin. Because of species differences, the immune reaction in a rabbit may also not match the response in humans.

The sixth new test uses cultures of human cord blood and mouse embryonic stem cells to detect low levels of white blood cells—a common side effect of cancer drugs. The test will speed up phase 1 clinical trials of cancer drugs, explains Hartung. Because there is no assay to assess the right initial dose of experimental cancer drugs, scientists now start with a low dose in animals and incrementally increase it till they get an adverse response. Another 9 in vitro tests are in the final stages of peer review and 25 more are in the pipeline.

The tests might improve on existing technology, but their use is also limited.

“Cells are not as metabolically active in culture as they are in vivo,” says Samuel Cohen, chair of microbiology at the University of Nebraska. Cells also don’t provide a picture of general metabolism. Animal models are more accurate when the liver can detoxify a drug and alter its potency, for example.

Still, a systematic comparison of existing methods is necessary, says Hartung. “We’re asking whether a method is actually doing its job and, if not, coming up with alternatives.”

The European Commission in 1991 established ECVAM in response to protests against the misuse of animals in research. Its mission has since evolved to improving toxicology methods. By law, once the agency validates a new technique, scientists within the European Union are required to use it.

Gunjan Sinha, Berlin

Despite doubts, containment plans for pandemic take shape

As the H5N1 avian flu virus continues its relentless march westward, scientists are scrambling to prepare for the possibility that it will mutate into a form that can jump between—and kill—humans. Top among the strategies is a plan to snuff out an outbreak right where it begins, but few experts believe that will work.

Quarantine and other measures limited outbreaks of the severe acute respiratory syndrome in China, but won’t contain influenza, says Yoshihiro Kawaoka, professor of virology at the University of Wisconsin in Madison (see page 489). “There’s no way, it won’t work. Influenza is different,” he says.

In August 2005, epidemiologists modeled outbreaks in Southeast Asia and concluded that, given early warning and enough Tamiflu, a human outbreak can be contained (Science 309, 1083–1087; Nature 437, 209–214). But in February, Harvard University researcher Marc Lipsitch argued that the virus is likely to jump to humans multiple times, making containment nearly impossible (PLoS Med. 3, e135).

“If [the jump] can happen in one place, it can happen in more than one place,” Lipsitch says. “If it is introduced into more than one site, containment won’t work.”

Still, the World Health Organization (WHO) is embracing containment in its strategy, and plans to fund it out of the avian flu monies pledged at a conference in Beijing in January. A draft containment plan released in March lays out guidelines for national authorities to investigate a cluster of ill people, as well as for launching a full-blown containment effort. The two-phase plan will focus first on tracing the chain of infection, giving antivirals to those closest to the ill, monitoring health and preparing hospitals for highly infectious patients. The second phase may include voluntary and involuntary quarantine, closing of schools, churches, public transport and borders, and the large-scale distribution of antivirals.

The pharmaceutical company Roche has donated 5 million courses of Tamiflu to be rushed to the site of an outbreak. The goal is to get the doses distributed within 21 days, a possible tipping point into chaos identified by the models.

Even the skeptics, including Lipsitch, say the plan is worth a shot. The strategy might buy time to make more vaccines, for instance, might slow the pandemic down, and might improve the infrastructure of the countries, notes Imperial College London epidemiologist Neil Ferguson, who published one of the August models.

“If there is a chance to stop a pandemic, we have responsibility to try it,” adds Maria Cheng, a spokeswoman for the WHO. “It is a worthwhile effort, even if it fails.”

Emma Marris, Washington, DC
NEWS IN BRIEF

Prayer lacks the power to heal, study finds

The largest and most rigorous study to explore the effect of prayer on healing found in March that appeals to a higher being do not necessarily aid recovery.

Researchers measured the effects of intercessory prayer, or the act of praying for another person from a distance, on 1,802 heart-bypass patients in six US hospitals. One Protestant and two Catholic groups prayed each day for 14 days as patients rolled into surgery. The researchers found that individuals who were prayed for suffered as many complications from bypass surgery as those who were not (Am. Heart J. 151, 934–942; 2006).

As public interest in matters of faith has surged, several scientists have sought to measure the effects of spiritual practice on health (Nat. Med. 11, 1259; 2005). But explorations of intercessory prayer have been controversial and criticized as scientifically flimsy. And a few well-designed investigations—including a Duke University study last year on 748 heart patients—found no health benefits (Lancet 366, 211–217; 2005). The latest $2.4 million study was led by scientists at Boston’s Mind/Body Medical Institute.—PB

AIDS rates in Africa may be overestimated

The AIDS epidemic in some African countries has been vastly overestimated, and may have skewed policy and funding decisions, researchers said in March.

Independent studies have determined that the rates of infection are considerably lower than those previously published by UNAIDS. In South Africa, for example, UNAIDS estimated that 21.5% of the population is HIV-positive. But ORC Macro, a research company funded in part by the US Agency for International Development, pegged that number at 16.2%.

The sharp difference raises questions about the UNAIDS monitoring system and the policy decisions based on its figures.

UNAIDS surveys rely on pregnant women who visit prenatal clinics as a measure of the general population. But the studies favor young, sexually active women in urban areas, whose rates of HIV tend to be higher than those of the entire population, researchers say. The newer studies instead survey entire countries.—EW

Extreme drug resistance to tuberculosis emerges

A super-resistant strain of tuberculosis (TB) has become prevalent worldwide, posing new obstacles in combating the disease, researchers reported in March.

TB afflicts 9 million people each year and kills 2 million, but can be treated effectively with the antibiotics rifampin and isoniazid. TB bacteria can become resistant to those drugs when individuals fail to complete the full six-month daily course, and the resistant strains can quickly be transmitted to others.

About 2 million people worldwide are infected with multidrug-resistant TB, which resists treatment by the two first-line antibiotics. The World Health Organization and the US Centers for Disease Control and Prevention have introduced a new category of extensively drug-resistant, or XDR, to describe TB strains that outmatch the first-line antibiotics as well as at least three of the six second-line drugs (MMWR Morb. Mortal. Wkly. Rep. 55, 301–305; 2006).

XDR strains prove fatal in at least one-third of cases, a mortality rate 13% higher than multidrug-resistant TB and more than six times that of routine TB. Nearly 350 cases of XDR were diagnosed worldwide between 2000 and 2004, accounting for 11% of all drug-resistant cases in industrialized countries.—BD

Yeast proves faster, cheaper source of malaria drug

Genetically modified yeast could yield a cheaper version of artemisinin, the most powerful drug available to treat malaria.

Artemisinin is made from the leaves of the sweet wormwood plant, Artemisia annua. The plant has been used in China for more than 2,000 years but supplies of the plant have not been able to match the spike in demand in recent years.

Researchers from the University of California in Berkeley added genes from the wormwood plant to the yeast Saccharomyces cerevisiae, inducing it to make artemisinic acid, which is just a few chemical steps away from artemisinin. The process is easy, inexpensive and nearly 100 times faster than extracting it from the plant, the researchers say. The San Francisco–based nonprofit Institute for OneWorld Health has already begun scaling up the process.

Because the malaria parasite has become resistant to most other available therapies, scientists have pinned their hopes on artemisinin-based drugs. But a course of artemisinin costs $2.40, well beyond the reach of people in the poorest parts of the world, who most need the drug. Malaria infects up to 500 million people and kills nearly 1 million each year, 90% of them in sub-Saharan Africa.—AM

Pigs to produce healthy fats

Cloned pigs that have been genetically modified to produce beneficial fats could one day give meat-eaters a means to a healthier diet, scientists say. The pigs, born in November 2005 at the University of Missouri, make their own omega-3 fatty acids, which have been linked to a reduced risk of heart attacks and improved brain function.

Researchers cloned embryos from pig cells altered to express the fat-1 gene, normally found in algae, plankton and roundworms but not in mammals (Nat. Biotechnol. 24, 435–436; 2006). The gene converts unhealthy omega-6 fats into omega-3 fatty acids. But it is not yet clear whether omega-3s in pork, which is high in cholesterol and saturated fats, are as beneficial as those found in oily fish such as tuna and salmon.

Before they could be made available commercially, transgenic pigs would need to be approved by the US Food and Drug Administration, a costly and unprecedented endeavor that could take years and engender strident opposition by consumer groups. Only one of ten male piglets initially cloned tested positive for the fat-1 gene, had enhanced omega-3 content and was healthy enough to be kept alive. A litter of eight was cloned from that piglet at the University of Missouri, and researchers plan to breed and distribute the piglets for further studies.—BD

News briefs written by Paroma Basu, Bruce Diamond, Apoorva Mandavilli and Emily Waltz.
The body snatchers

Rising demand has created a thriving market for human body parts—and not all of it above ground. Emily Waltz explores the unsavory world of tissue trade.

For 58 years, Alistair Cooke enchanted his radio audience. A Brit who lived in New York, Cooke regaled listeners in the UK with stories about Americans and was honored for bridging the distance between the countries.

In March 2004, one week after he announced his last broadcast, Cooke died of lung cancer in his New York home. He was 95. As his listeners mourned, his family sent his body to be cremated at a local funeral home.

But the ashes that came back were not from Cooke’s body.

In December 2005, Cooke’s family learned that his body had been surgically plundered and the pieces sold to different bidders. A body brokerage company had harvested his bones, falsified his medical records—claiming he had died at 83 of a heart attack—to make them more marketable, and then sold them to at least two tissue banks.

COOKE’S was one of more than 1,000 bodies allegedly stolen by the company, New Jersey–based Biomedical Tissue Services. Prosecutors say the company and the funeral home, Daniel George & Son, made millions of dollars harvesting pieces of the cadavers, instead stuffing bodies for burial with broomsticks and piping. An investigation is ongoing.

The gruesome case, which dominated headlines for weeks, is only the latest instance of body snatching in the past few years. Required for education, transplant and research, human tissues are in increasing demand. In the flourishing underground market, a single cadaver sold for its parts can fetch up to $200,000. Individual parts can make their way through several brokers before ending up in retail stores, fraternity houses, art exhibitions, the online auction eBay—or research labs.

“This is a dirty market,” says Glenn McGee, director of the Alden March Bioethics Institute at Albany Medical College in Albany, New York. “The materials for scientists depend on a supply chain that begins with guys in dark suits expressing strong sympathies.”

Hunting for human tissue

Too often, scientists don’t ask where the samples they use come from. But the implications of their ignorance go beyond ethics. As in Cooke’s case, unscrupulous body brokers can tamper with facts and seriously skew a study’s outcome—or worse, a transplant recipient’s fate.

Scientists can’t just rely on the government either. Following some particularly gruesome cases, the UK in April launched a stricter set of laws on handling human tissues. But in the US, the Food and Drug Administration (FDA) monitors only organs used for transplant, not those used for research or education, letting the onus fall on the researcher.

Tissues for research are available from any number of places, but most researchers aren’t aware of their options. There is no central clearinghouse nor a catalog of outlets, so researchers must find their own way. Scientists who work at hospitals can get tissues from surgeons there—a fairly common practice—as long as they follow rules of confidentiality. They might even share tissues samples, trading the pieces they don’t need.

State anatomical boards and nonprofit donation programs also contribute. Nearly all medical schools have a body donation program, and some allow scientists access to the bodies their students don’t dissect. Some hospitals also use organ procurement organizations. When someone dies, these organizations first try to find a transplant recipient, but if no match can be found quickly, arrange for a researcher to get the organs.

But that route is far from reliable.

“You can’t predict when people will die,” says Eric Liu, a clinical research fellow at the US National Institute of Diabetes, Digestive and Kidney Diseases. “If it has to be human tissue and you want it to be fresh, you have to be ready to accept it and process it at all hours.” Liu, who uses pancreatic tissue in his studies, says he has on more than one occasion had to process samples in the middle of the night.

With an unpredictable supply of bodies, scientists, especially those in need of specific tissues, sometimes turn to for-profit companies who work with the funeral industry. But approaching these sources is risky, experts caution.

“The most egregious behaviors involve individuals in the profit-for-death industry that are taking advantage of their unique situation,” says Todd Olson, director of the body donation program at the Albert Einstein College of Medicine in New York. “This is one of the most secretive groups of people,” he says.

Those who work in the death industry don’t have to open their books to the public so they can reap enormous profits—none of which reach the donor’s family—from scientists and funding agencies.

Undying market

Illegal body trade has long been a lucrative proposition. In the 1800s, the UK and the US saw a sharp rise in the number of medical schools that needed cadavers for their students to dissect. But at the time, dissection was an option only for the poor, who couldn’t afford a proper burial, and not for the middle and upper classes.

With the rising demand, medical schools began collecting unclaimed bodies from poorhouses. When there was a shortage, the schools would hire body snatchers to rob graves. In the 1820s, two Irishmen, William Burke and William Hare, reportedly murdered 16 people and delivered the corpses to a doctor for payment.

By 1950, advances in science encouraged people for the first time to donate their bodies. Vaccines for polio and rabies, anesthesia for childbirth and antibiotics all led people to
believe that science could create a better world, says Michael Sappol, a medical historian at the National Library of Medicine.

But the demand outpaced the rise in donations. Researchers found new ways to use human tissues in their work. Companies wanted body parts to test new surgical devices and diagnostics. Continuing medical education courses needed cadavers to train surgeons. In recent years, some large-scale projects such as mapping the human genome boosted the market even more.

“Better genetics means that diseased tissue can now be used to look for markers that indicate risk factors for disease. So trash now has value as a source to develop genetic tests,” says Arthur Caplan, a bioethicist at the University of Pennsylvania. “This leads companies to want to build big biobanks of rotten pancreases, crummy lungs, failed hearts and burnt-out livers.”

With the clamor for tissues, even scrupulous handlers of cadavers were tempted to try and profit. Some of the most infamous cases surfaced in the courts and the news in the last few years.

In March 2004, for example, Tulane University officials discovered that seven corpses the university sold to a broker were blown up in landmine tests. University officials said they sold the cadavers for $7,000 to the National Anatomical Service, a New York–based distributor. The organization then sold the bodies for nearly four times the amount to the US Army. Families of the donors were outraged that the bodies had not been used for science, but university officials pleaded ignorance.

An even more shocking case emerged in 2004, when Henry Reid, director of the body donation program at the University of California in Los Angeles (UCLA) was accused of trafficking as many as 800 bodies into the black market. Over six years, Reid had allegedly made more than $700,000 allowing a broker to pick through the bodies for nearly four times the amount to the US Army. Families of the donors were outraged that the bodies had not been used for science, but university officials pleaded ignorance.

As more tales of thievery surface, researchers say they are concerned that people will stop donating their bodies to science. “It’s a big worry,” says David Burr, chief of anatomy at Indiana University School of Medicine. “We don’t have an overabundance of bequeathals. Our programs work off good public relations, so when something happens at UCLA, it’s a problem for us too.”

Loose laws

With so much at stake, why have the laws remained so lenient? The reason, bioethicists say, is hard lobbying by those in the death industry and legislators’ reluctance to deal with the icky subject matter. “It’s a business with a nefarious history and nobody wants to talk about it,” says McGee.

In the US, the FDA regulates tissues used for transplant and requires disease screening and medical history of the donors. But no federal law or agency regulates the sale of human tissue intended for research or teaching. State laws govern the trade, but are based on loose wording of what’s known as the Uniform Anatomical Gift Act of 1968.

The act is now up for revision, although it is unclear exactly what might change. As it stands, the law requires consent from the family or the donor to use the body for science. It also prohibits anyone from selling human tissue for profit.

But vague wording in some sections allows much room for interpretation. For example, tissue brokers are allowed to recoup “reasonable” costs for shipping and handling, but the law does not define what is considered reasonable. Donated bodies must be used for science in some way, but ‘science’ is an undefined catch-all category.

Other countries have even fewer rules. Until April, hospitals, coroners and anyone else who handled cadavers in the UK did not have to get formal consent to dissect the body. The UK’s Human Tissue Act of 2004, which went into effect in April, requires everyone who handles cadavers to get a license and to ask for written consent from the families. The act also set up a Human Tissue Authority to inspect tissue brokers on site.

But the best solution, experts say, is not more government oversight.

“The government will just screw it up,” says Kenneth Iserson, director of the Arizona Bioethics Program at the University of Arizona. “They will overregulate in some bizarre fashion that will make it more difficult than it already is.”

Instead, experts say, organizations that buy bodies should require total transparency from suppliers. These groups should demand documentation on how handlers store and transport the bodies, and how much money they received in return.

Some also suggest that funding agencies and institutional review boards require more explanation from researchers on how they plan to acquire their tissue samples.

Few researchers routinely ask questions about a tissue’s origin or about the middlemen along the trade route who could have profited. But they might pay the ultimate price if there are unscrupulous brokers involved. For example, if a scientist studying bone loss in aging women uses tissue from a 75-year-old postmenopausal woman that is labeled as tissue from a 42-year-old premenopausal woman, the sample could clearly skew the results.

“If I could give one piece of advice to bench researchers, I’d say ask for the source,” says Olson. “If the funeral industry was involved, you need to ask more questions.”

Emily Waltz is an intern at Nature Medicine.
Yoshihiro Kawaoka

If Yoshihiro Kawaoka owned a country, its citizens would be well protected from a bird flu pandemic.

Confronted with a pandemic, Kawaoka says he would close his country’s borders and release a vaccine based on the live, but weakened, bird flu virus. Some people might fall ill from the vaccine strain, but far greater numbers would benefit. “The immune response provided by live virus, that is going to be the one that really protects humans,” Kawaoka says.

He is only half-serious. Kawaoka knows that closing borders is impractical and would at best only stall the pandemic. But when it comes to a vaccine, he knows of what he speaks.

Kawaoka engineered a method to generate entire viruses from genetic sequences, a technology that’s now used to make flu vaccines. He has published paper after high-profile paper describing what makes certain flu viruses lethal and how they acquire resistance to available drugs. Most recently, he suggested that the H5N1 virus prefers to bind receptors far down in the lungs, making it more difficult for the virus to jump between people (Nature 440, 435–436; 2006).

Since 1999, Kawaoka has juggled dual appointments at the University of Tokyo and the University of Wisconsin in Madison. Full-sized labs at each institution churn out top-notch publications, 27 in 2005 alone.

“I’m glad that I work with him and don’t have to compete with him,” says Heinz Feldmann, chief of special pathogen programs at Canada’s National Microbiology Laboratory, and Kawaoka’s collaborator on Ebola virus research.

Kawaoka became interested in Ebola after reading The Hot Zone, the only English novel he says he has ever read. But soon after he began working in the field, “Yoshi really came on the scene with a bang,” recalls Tom Geisbert, chair of viral pathology at the US Army Medical Research Institute of Infectious Diseases in Fort Detrick, Maryland.

How Kawaoka has the energy to do so much is a mystery. He doesn’t eat much, sleeps even less and is perpetually jetlagged. To keep up his dual appointment, he often travels to Tokyo, sometimes for just a day.

Even as a postdoc at St. Jude Children’s Research Hospital in Memphis, Tennessee, Kawaoka was in the lab when the cleaning lady arrived in the early evening, would go home to sleep at some point and be back again, ready to start the next day, before she left. “We’re all amazed at how he can physically manage to function so well in two different time zones,” says Krisna Wells, who has worked with Kawaoka since 1987. “Personally, I don’t think he sleeps.”

Still, running two labs gives Kawaoka the best of both worlds.

His appointment at the University of Tokyo’s prestigious Institute for Medical Sciences guarantees that his lab is always supplied with the best Japanese students. And Wisconsin allows those students to run experiments with recombinant DNA, which is under strict regulation in Japan.

But the dual appointment also has its share of headaches.

“Often I hear from Japanese that we, meaning Japanese, should do the work that sends a message to the world,” says Kawaoka. “But it doesn’t matter whether I do this work in Japan or the US or wherever. If people make comments, I don’t say a word. I don’t care what other people think.”

Kawaoka began his career with a stint in veterinary school at frosty Hokkaido University, followed by graduate degrees in microbiology and bacteriology. After his mentor in Hokkaido introduced him to Robert Webster, already a leader in influenza work, Kawaoka went to humid, mosquito-infested Memphis—and stayed there for 14 years.

In April 1983, four months before he arrived in the US, an H5N2 flu virus was sickening chickens in Pennsylvania. At first, the virus was only mildly pathogenic. But in October that year, it suddenly began killing chickens in large numbers.

Webster took Kawaoka to the early-morning poultry markets in New York City to sample the birds that were the source of the Pennsylvania virus. “[Speaking] as a mentor, he was the best student ever. He was brilliant,” Webster says.

When the researchers compared the April and October strains, they found that the milder strain had become more pathogenic after just a single mutation in the hemagglutinin gene (Virology 149, 165–173; 1986). That work, along with data from an outbreak in Mexico in 1993, established the concept that all highly pathogenic viruses are derived from nonpathogenic strains.

“If people make comments, I don’t say a word. I don’t care what other people think.”

Webster recalls that when Kawaoka and his family first arrived in the US, they were polite and proper, as most Japanese are. But the first time they visited Webster’s house, their son, then two years old, picked up a duck-shaped cushion off the sofa and hurled it right at Webster. “We were highly amused. But they were embarrassed out of their minds,” Webster recalls.

“[Kawaoka] has since lost that formality somewhat.”

One year, Webster’s wife taught Kawaoka to wallpaper the rooms. Ever the eager student, Kawaoka mastered the skill and now inspects the wallpaper in his hotel rooms. “I watch the seams, you know, I can do it better. I can match the pattern,” he says. “Even if lose my job some time, I can maybe put wallpaper up as a career.”

Perhaps then he would work a little less.

Last year, on the twenty-fifth anniversary of his marriage, Kawaoka found himself once again on a plane to Japan. His wife, Yuko, whose father worked 9-to-5 shifts and came home for lunch, was less than thrilled. “She doesn’t care about me publishing high-profile papers. What she wants is for me to stay home,” he says.

Kawaoka promises to retire at 65 and stay home doing nothing, perhaps only listening to music and reading novels by the Japanese author Mangetsu Hanamura. Sensitive about his English speaking skills—regularly criticized by his students at the University of Wisconsin—he says he would probably want to die in Japan, where he wouldn’t have to worry about making sense to the doctors.

Not surprisingly, Japanese would also be the language of his choice in any country he owns. Perhaps, Kawaoka says laughing, the country would be populated only with women. And what would it be called? “Yoshi’s country, of course.”

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