NEWS IN FOCUS

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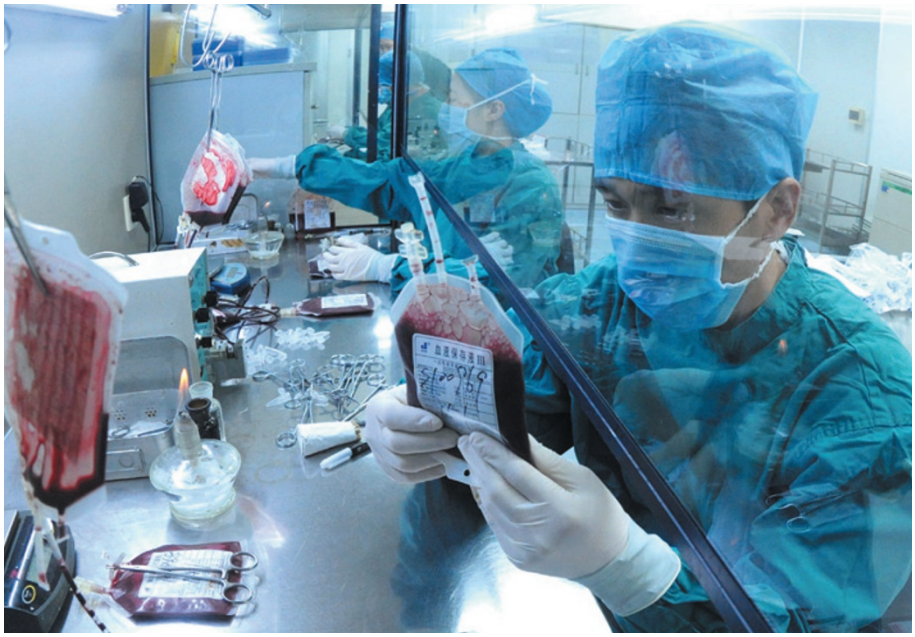


It's boom time for firms selling stem-cell treatments, such as those derived from umbilical blood.

REGENERATIVE MEDICINE

China's stem-cell rules go unheeded

Health ministry's attempt at regulation has had little effect.

BY DAVID CYRANOSKI

Three months after the Chinese health ministry ramped up its efforts to enforce a ban on the clinical use of unapproved stem-cell treatments, a *Nature* investigation reveals that businesses around the country are still charging patients thousands of dollars for these unproven therapies.

The clinics operate openly, with websites promoting the treatments for serious disorders such as Parkinson's disease, diabetes and autism, and attract thousands of medical tourists from overseas. They advertise case studies of individual patients who they say have benefited from the treatments, and some have clinics in major hospital complexes, giving them an air of mainstream acceptance. Stem-cell experts contacted by *Nature* insist that such therapies are not ready for the clinic and say that some may even endanger patients' health. But the Chinese government is struggling to enforce its ban.

In May 2009, the Chinese Ministry of Health classified stem-cell treatments as Category 3 medical technologies, defined as "high risk" and requiring the approval of a technical audit board before use. So far, no approvals have been granted. Despite this, "one 2009 estimate put the number of stem-cell companies based in China at around 100", says Doug Sipp, a stem-cell ethics and regulation researcher at the RIKEN Center for Developmental Biology in Kobe, Japan. In his view, "even after the reform efforts by the Ministry of Health, the industry apparently continues to grow."

In January, recognizing the worsening situation, the health ministry announced a package of rules for the industry. Organizations using stem cells must register their research and clinical activities, the source of the stem cells and ethical procedures. The ministry asked local health authorities to halt any unapproved clinical use of stem cells in their regions. And it called for a nationwide moratorium on new clinical trials for stem-cell therapies, adding that patients in existing clinical trials should not be charged.

So far, however, the ministry's clampdown has proved ineffective. According to a Ministry of Health spokesman, not one clinic has registered in the required way, and *Nature* has found that many stem-cell clinics continue to offer treatments. Shanghai WA Optimum Health Care, for example, which has plush headquarters in a gated estate in one of the wealthiest areas of central Shanghai, claims success in using stem cells derived from umbilical cord or adipose tissue to treat a range of disorders, from autism to multiple sclerosis. Tony Lu, a member of the company's science and technology board, says that four to eight injections of such cells can treat Alzheimer's disease, at a cost of 30,000–50,000 renminbi (US$4,750–7,900) per injection. According to the company's senior patient-liaison officer, Karina Grishina, autism can be treated with an adipose-tissue-derived cell injection for 200,000 renminbi, followed a few days later by a 50,000-renminbi injection of umbilical cord cells.

In Changchun, Tong Yuan Stem Cell claims to have treated more than 10,000 patients with a variety of disorders, including Parkinson's disease. A representative says that it also offers a one-year, four-injection autism treatment protocol using stem cells from aborted fetuses. Meanwhile, Beijing Puhua International Hospital's Stem Cell Treatment Center offers a four-to-five-injection protocol for autism, costing 205,000 renminbi.

Those clinics all claim success in treating patients, but none has published data from controlled clinical trials. Zhou JingLi, chief neurologist at Beijing Puhua, says that many of the company's autistic patients have shown marked improvements in their condition a couple of weeks after treatment. She agrees that controlled clinical trials are needed to ▶

verify the efficacy of their treatments. "But," she asks, "who's going to pay?" She adds that first-hand experience with patients is enough to show that stem-cell treatment is worthwhile. "First, it's safe; second, it's effective. We know that," she says.

Leading stem-cell scientists think otherwise. Commenting on Tong Yuan's treatment for Parkinson's disease, Oliver Cooper, director of the Stem Cell Facility of the Neuroregeneration Institute at McLean Hospital in Belmont, Massachusetts, and a specialist in Parkinson's disease, says, "The products offered by Tong Yuan may provide anecdotal, poorly controlled, transient improvements in the patients, but Parkinson's-disease patients need long-term therapies."

"There are neither scientific nor clinical data to support the long-term benefits of haematopoietic- or neural-stem-cell therapies for Parkinson's patients," he adds. "In fact, it's not clear if the infused cells will survive for more than a few days in the patients."

Meanwhile, neurobiologist Ricardo Dolmetsch, an autism researcher at Stanford University in California, says, "The consensus in the autism research community, as well as in the stem-cell community, is that there is no scientifically valid reason for using stem cells to treat autism spectrum disorders". He worries that, without the proper safety studies in place, the treatments could "lead to serious complications like cancer and autoimmune disease".

In addition to anecdotal case studies, some Chinese stem-cell companies bolster their reputations by claiming to have connections with leading politicians and scientists. A glossy 'information memorandum' from Shanghai WA Optimum Health Care contains pictures of staff with various local- and central-government figures, including Li Keqiang, the powerful executive vice-premier of the State Council who is tipped to succeed Wen Jiabao as China's next premier.

It also lists Li Lingsong, director of the Peking University Stem Cell Research Center, as a member of its science and technology board. Li denies this. "I have so far nothing to do with WA," he told *Nature*, adding that he has asked the company to remove his name. WA also claims a strategic alliance with Harvard Medical School, although neither the medical school nor the Harvard Stem Cell Institute is aware of any such connection. Likewise, the University of California, Irvine, where WA claims to have research facilities, denies any formal relationship.

When pressed, all of the stem-cell clinics approached by *Nature* said that they were aware of the government regulations, and that they were necessary — but only for other clinics that were not operating safely. Most emphasized that their own businesses were entirely legitimate. *Nature* did find one company, Shanghai Puhua, which says that it has already stopped offering stem-cell treatments to comply with government regulations. And Beijing-based Wu Stem Cells will probably do likewise for the same reason, says company director Cheng Bo.

Bioethicist Zhai Xiaomei at Peking Union Medical College in Beijing, a member of one of the government's technical audit boards, was surprised to hear that any stem-cell companies were still operating. She says that the regulations are "absolutely clear" that companies must not administer unapproved stem-cell treatments.

A Ministry of Health representative told *Nature* that it was aware of the problem, and that it would be making greater efforts to clean up the stem-cell business.

Asked how WA operates despite the ministry's ban, Lu describes the regulations as "a grey area". Grishina agrees: "We're in China, so there are different stipulations." ■ SEE EDITORIAL P.141

BIOSAFETY

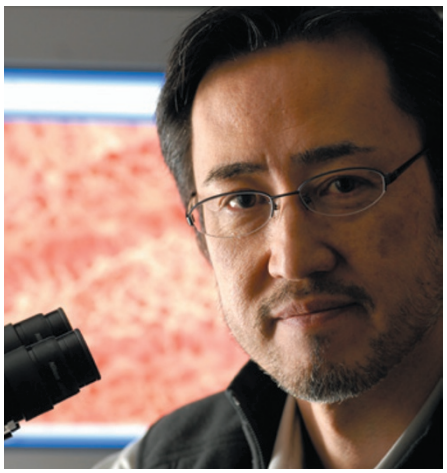
Post-mortem on mutant flu

Virus papers get green light but controversy highlights lack of global rules on biosafety.

BY DECLAN BUTLER

The dust is beginning to settle on the months-long controversy over two studies in which the H5N1 avian influenza virus was modified to be transmissible between mammals. But scientists and authorities still need to address the lack of international oversight for studies in which pathogens are deliberately made more dangerous, speakers emphasized at a two-day meeting held last week at the Royal Society in London. The meeting brought together scientists, research funders and experts in security, bioethics and foreign policy, just days after the US National Science Advisory Board for Biosecurity (NSABB) revised its earlier stance and recommended publication of the two studies.

In December 2011, the board recommended redaction of experimental details of the studies, on the basis of concerns about bioterrorism and the increased likelihood of accidental release of the viruses. But after considering revised versions of the manuscripts on 29–30 March, the NSABB voted unanimously in favour of full publication of the paper submitted to *Nature* by Yoshihiro Kawaoka of the University of Wisconsin–Madison, and 12–6 for publication of the content (although not the specific wording) of the paper submitted to *Science* by Ron Fouchier of the Erasmus Medical Center in Rotterdam, the Netherlands.



Yoshihiro Kawaoka can now publish his flu study.

J. MILLER/UNIV. WISCONSIN-MADISON

Kawaoka presented his findings for the first time at the Royal Society meeting (see *Nature* http://doi.org/hsn; 2012), but Fouchier gave only a summary of his, saying that a more detailed description was prohibited by Dutch export-control laws, which require a permit to disseminate samples of, and information about, certain dangerous pathogens.

In December, the NSABB said that the information in the papers could help H5N1 surveillance efforts and so should be made available to experts on a need-to-know basis. A major factor in the board's change of heart was that subsequent international discussions concluded that there was no practical way to selectively share the data, and that national export controls may restrict distribution anyway, says Michael Imperiale, a virologist at the University of Michigan in Ann Arbor and a member of the NSABB.

This left the board with the stark choice of publishing either all or none of the research, with publication becoming "the only way for public-health authorities to know what to look