second, passive immunisation that uses antibodies directed only to the fibrillary form of the a-β peptide, not to the soluble, non-toxic precursor, which Chain believes could interfere with other activities in the body. 'The advantage of passive therapy is that it does not require immune activation or any adjuvants,' he said. One drawback, however, is that it must be given repeatedly because the body gradually removes the antibodies.

Neurochem in Saint-Laurent, Canada, is taking a different approach to overcome the problems of inflammatory reactions and an insufficient immune response. Their compound triggers a response to only a small portion of a-β-42, so antibodies will prevent the formation of amyloid fibrils while avoiding other, unwanted side effects, Francine Gervais, vice president of research and development, explained. 'Amyloid β is a protein that is normally present in the blood in soluble form,' Gervais said. 'However, we do not know its non-pathogenic function—only that it is important because it is conserved in many species.' What is not natural is when it deposits in the brain, so Neurochem's vaccine triggers the immune system to recognise only the soluble form of the protein and remove it before it forms fibrils. It should prevent plaque build-up, but is not expected to attack extant plaques, Gervais said. She envisions that a single initial vaccination would be needed, and that patients would receive a 'booster' every few years.

Gervais does not believe, however, that one vaccine will necessarily work for all those at risk or with early-stage disease. 'Alzheimer's disease has a number of different risk factors besides age—notably, apo-E status and other genetic factors, and a history of head injury,' Serge Gautier, of the Center for Studies in Aging at McGill University in Montreal, Canada, and a member of Neurochem's advisory board, said. 'Therefore, a number of approaches besides vaccines are likely to be necessary to treat the range of patients.'

One approach is to lower the amount of a-β-42 in the brain rather than attacking plaques directly. This is simplified by the fact that a-β crosses the blood–brain barrier easily, especially in Alzheimer's patients where it is more permeable, according to Gautier. This could allow antibodies and other protein-binding molecules to act as a 'sink' for a-β-42 by removing it from the bloodstream, thus lowering its concentration and its ability to form plaques in the brain.

This was shown to be a promising approach last summer when David Holtzman from Washington University in St Louis, MO, reported that a monoclonal antibody directed against the central domain of a-β caused a 1000-fold increase of the peptide in the blood of transgenic Alzheimer's mice and prevented further deposition in the brain. 'This "sink" effect is due in part to a change in a-β equilibrium between the central nervous system and plasma,' described Holtzman who is collaborating with Eli Lilly that produces the antibody. The goal of the study was to determine whether exogenous molecules could change this equilibrium, given that endogenous proteins, such as apoE and apoJ, can influence the transport of a-β between the brain and plasma, Holtzman said. He thinks that apart from antibodies, other proteins or molecules that bind a-β may serve to facilitate clearance of the soluble peptide from the brain.

Despite the drawback in Elan's clinical trials, most researchers are still optimistic that an immunotherapeutic approach will play an important role in treating and possibly preventing Alzheimer's disease. And the results from Elan's investigation should provide further knowledge of how to overcome this debilitating disease.

Vicki Brower

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Will they throw the bath water out with the baby?

The US Congress is still debating whether to outlaw cloning humans

There appears to be no historical precedent for what a committee of the illustrious US National Academy of Sciences (NAS) did in January: it called for outlawing a certain kind of scientific endeavour. The reaction of US scientists to the promulgation of a ban was equally unprecedented: they went along with it—meekly.

The NAS committee recommended that cloning human embryos for procreation purposes should be prohibited by law and that violations should be punished severely. In reality, this was a last-ditch attempt to salvage another kind of human cloning: embryo creation via somatic cell nuclear transfer with the aim of generating stem cells for disease research and, ultimately, therapy.

The report drew an emphatic distinction between two forms of cloning that are all too often lumped together: reproductive and therapeutic. Reproductive human cloning, it said, should not now be practised because animal research shows that it is dangerous to the potential mother and baby—and likely to fail. But these strictures, it argued, did not apply to nuclear transfer for the production of stem cells, which should be allowed to proceed with no restrictions.

Science lobbyists such as the gigantic Federation of American Societies for Experimental Biology, representing 21 research

organisations with 60 000 members, immediately endorsed the report and its call for a legal ban on reproductive cloning. The Association of American Medical Colleges (AAMC), a heavyweight research lobbying consortium, followed suit, although in the past it had urged a different approach, a voluntary moratorium on reproductive cloning. Tony Mazzachi, an AAMC official, called the report 'A very thoughtful, nuanced discussion and recommendations—and it parallels almost exactly AAMC's position.'

The NAS recommendations may be somewhat more palatable to researchers because they called for what is known in the USA as a sunset provision: the report asked that any ban be reviewed within 5 years to reassess the current scientific and medical judgement of the risks. 'There's a lot of people who have said to me that they're very worried about allowing legislation which would contain a ban because, just as ethicists worry about a slippery slope, so do scientists,' recounted Irving Weissman, noted cancer biologist at Stanford University (CA), who chaired the NAS committee. 'But I said, "You know, this is science *and* medicine, and we do have bans in medicine."' Weissman cited the Nuremberg Code, with its declaration that human experimentation is not permissible when the risks are substantial. 'The risk for this kind of experimentation is far more than substantial,' he said.

'There are some who will cynically say scientists recognise that to complain about restrictions on research on reproductive cloning would be a wonderful way of enraging the American public,' said Thomas Murray, who heads The Hastings Center, the bioethics research organisation. But most scientists share the public's abhorrence of cloned babies, he said, a feeling exacerbated by disgust at the champions of cloning who claim to be scientists. 'There have been enough pronouncements from kooks, nuts, goofballs and con men—including some at the Academy hearing where that report got written—that the result has been plain panic,' commented Arthur Caplan, who directs the Center for Bioethics at the University of Pennsylvania. He is referring to Severino Antinori, Brigitte Boisselier and Panayiotis Michael Zavos. Antinori, who is at the Tor Vergata University in Rome, is also scientific director of the International Research Association for Human Reproduction. Boisselier directs Clonaid, the first human cloning company, which is connected to the Raelians, an obscure religious group. Zavos is an

emeritus reproductive physiologist at the University of Kentucky and practitioner of assisted reproduction. All have declared their immediate intention to make babies via cloning, even in the face of tough questions from scientists about their competence to carry out the plans. Caplan blames the media for not doing enough to debunk the claims of the would-be cloners. 'I don't consider them credible in the least. But they seem to have frightened people, they seem to be steering public policy by terror.'

Many who oppose human cloning believe it is wrong whatever its ultimate justification, a point of view that has turned activists on both the left and the right into strange bedfellows. On the left are feminists concerned about risks to women, environmentalists concerned about risks to ecosystems, and groups such as the Council for Responsible Genetics concerned about what it calls the 'commodification' and 'corporatisation' of human reproduction. Most of the resistance, of course, is from the right, emanating largely from that perennial American gadfly, the right-to-life lobby.

US state legislatures are currently debating outlawing all types of human cloning. Proposals include punishing reproductive cloning with fines of $10 million and 10-year prison terms. To date, only Virginia has a total ban; other states are proposing to permit therapeutic cloning. The Wisconsin state senate passed such a bill in January; Wisconsin is home ground for the University of Wisconsin's James Thomson, the godfather of embryonic stem-cell research, and of the WiCell Research Institute, the source of five of the limited number of embryonic stem-cell lines approved for federally funded research last summer by President Bush.

State bills, however, are likely to be overridden by federal legislation. The US House of Representatives last year threw the bath water out with the baby by passing a ban on both therapeutic and reproductive cloning. In the US Senate, three bills of varying stringency are scheduled for debate and perhaps a vote in March this year. Science lobbyists are hoping for the passage of one of the two that would permit therapeutic cloning while outlawing reproductive cloning, even though they contain no sunset provisions, and thus any ban would be permanent. But the prospect of bartering cloned babies for human embryonic stem-cell research does not look good, since currently a total ban appears to be in favour. 'It's going to be a tough battle,' acknowledges David Moore, who tracks legislative matters for the AAMC. Even if the Senate voted with the science lobby, final legislation would have to be worked out in conference with the House, which has displayed no inclination to compromise on its desire for a total ban.

Meanwhile, human embryonic stem-cell research looks set to proceed in Europe. A brief judicial scuffle in England has been resolved, allowing therapeutic cloning to continue. Last November, the High Court ruled that the restrictions Parliament had placed on cloning in 2000, which would have forbidden reproductive cloning while permitting therapeutic cloning, were invalid. The restrictions amended a 1990 law pertaining to embryos derived from fertilisation and so, the High Court said, did not apply to cloning. UK pro-life

The US House of Representatives last year threw the bath water out with the baby by passing a ban on both therapeutic and reproductive cloning

activists were hoping the ruling would mean a ban on all human embryo cloning in the UK. But then, in January, 2002, the British Court of Appeals reversed the High Court decision, saying that Parliament would have included human embryo cloning in the 1990 law if they had known it was on the horizon.

France is debating a bill that would ban both reproductive and therapeutic cloning and impose 20-year prison sentences on violators. But the bill would allow research on 'surplus' frozen embryos from fertility clinics. Like lawmakers everywhere, French politicians know that endorsing any position on cloning will inevitably alienate some of their constituents, so any law is unlikely before French elections this spring.

Last summer, France joined with Germany to ask the United Nations for an initiative banning human reproductive cloning. But even Germany, where the Nazi spectre hovers over all human experimentation, and where human embryo creation for research purposes continues to be banned, has decided that importing human embryonic stem cells for research is permissible. At the end of January, 340 lawmakers voted in favour of restricted imports, and 106 favoured unrestricted imports and eventual production of the cells in Germany. This compared with 265 lawmakers who wanted to ban stem-cell imports completely, a stance supported by both the Roman Catholic and Lutheran churches. Government officials were divided along party lines, with Chancellor Gerhard Schroeder favouring limited imports and the Federal President opposing it. Calling the decision 'necessary for German scientists', Anna M. Wobus, a researcher working with human stem cells at the Institute for Plant Genetics and Crop Plant Research in Gatersleben, Germany, noted that the vote was a compromise between scientific aims and ethical and social concerns. She said that it will only be possible to decide whether embryonic cells are better than somatic cells for stem-cell research with further investigation; the research must come first.

> Research carried out in countries where the use of human embryos is permitted will be key to solving the legal problems elsewhere and rescuing therapeutic cloning

Others agree. Caplan declared that research carried out in countries where the use of human embryos is permitted will be key to solving the legal problems elsewhere and rescuing therapeutic cloning, especially in the USA. 'I think we'll get some answers, they'll just come more slowly. Answers will come from England or Sweden or Australia about the potential. If the potential looks very strong, then I think the demand from patients will overwhelm any moral objections on the pro-life side. It's a little hard to argue potential cure against real harm to a human embryo. It's not so hard to argue the moral priority of curing your child of diabetes or getting somebody out of a wheelchair—if it works—against that same standard.'

Tabitha M. Powledge

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A right for family planning

The benefits of contraception for women's health and social status

Once upon a time in babyland, where babies pop out of giant, baby-making flowers, Mr Stork picked up a cheeky baby for early-morning delivery. But this time, things would be different. Close to his final destination, Mr Stork bumped into a huge brick wall. He flew back a little, shook his dizzy head, gathered all of his strength, and surged into the brick barrier once more. To cut the story short, the persistent bumping would have gone on forever if someone had not told poor Mr Stork that from now on, baby home-delivery would be carried out upon request and according to the will of the parents. The well-known baby deliverer had hit the wall of contraception, the most effective method of controlling reproduction.

Contraception was indeed the Big Bang in the evolution of baby-making strategies. In Western countries, it is now as easy to get effective contraception as it is to get an anti-biotic against, say, an ear infection. Women can walk into their doctor's surgery, get a prescription that they hand in at the nearest pharmacy and receive a pack of pills that—if taken appropriately—will effectively prevent pregnancy. Although contraception has its roots in ancient times, the ease with which modern contraceptives can be used and their efficiency have made them a highly attractive measure for women to improve their well-being. Indeed, given the complications and stress that a pregnancy can entail for a woman, controlling her number of children has become one of the major measures to ensure her long-term health and quality of life. What is more, modern contraception has given women the means to rise above breeding and child-bearing and fight for their rights and equality. As Natalie Angier, science reporter for the *New York Times* and author of the book *Women*, bluntly put it, 'Women, like all female primates, have two basic goals: to control their reproductive lives and to have access to resources. A woman who is prevented from doing either is less free than a female chimpanzee or gorilla.'

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