

Trying to shake Japan's faith in forecasts

Tokyo

THE future of Japan's huge national research effort to predict earthquakes, which has run for nearly three decades and consumed thousands of millions of yen, is being questioned for the first time by scientists here.

Japan is practically the only country in which earthquake mitigation and hazard reduction takes a back seat to predicting the next big one. Yesterday (8 April), scientists who are critical of that emphasis were expected to have their first chance to modify its course at a meeting in Kyoto of a newly formed subcommittee of the Science Council of Japan, an academic advisory body to the government. But even they are not optimistic about their chances of success.

Standing firm against any attempts to open up the system to outsiders are a handful of senior seismologists, who have been in the earthquake prediction business since the 1960s. This group have effectively by-passed external review by holding a series of closed meetings over the past few months to draw up their own internal review of the research for the government, in much the same way as they have done for the past 30 years. The review process now unfolding provides insight into how small groups of powerful academics can exert enormous influence over government funding of research in Japan.

The earthquake research programme is one of Japan's largest and oldest national research projects. In the past 17 years, according to government statistics, the programme has consumed almost 100,000

million yen (US\$700 million), and currently receives about \$50 million a year (see figure). But, the government figures are deceptively low, because they do not include the salaries of the 500 or so researchers in various government research organizations who are involved in earthquake prediction.

Last year, US geophysicist Robert Geller of Tokyo University sent shock waves through the earthquake prediction

In February's issue of the semi-government publication 'Japanese Scientific Monthly' (*Gakujutsu Geppo*), Uyeda describes the growing disillusionment among Japan's seismologists with the present state of prediction research in Japan, which consists mainly of collecting huge amounts of data in the hope that some reliable 'precursor' of earthquakes will be found. That approach has largely been abandoned in the United States and elsewhere after the failure in the 1970s to find such precursors. Uyeda suggests that perhaps the only way to reinvigorate the research community in Japan is to create "a crisis" and to cut the government budget for the programme to "one-tenth its present size".

The new science council subcommittee, which met for the second time this week in Kyoto, was set up last October partly in response to such criticisms. The 27-man subcommittee includes Geller and several other critics, as well as senior leaders of the earthquake prediction programme. At the urging of the critics, the agenda for this week's meeting calls for a new "blueprint" for earthquake prediction to replace the one that set the present programme on its course in the 1960s.

The discussions in Kyoto, however, are not expected to change the course of earthquake research in Japan. A smaller but much more powerful eight-man committee of senior seismologists, many of whom are also on the new Science Council subcommittee, have met six times behind closed doors since October and have already produced a draft review of the earthquake prediction programme, now in its sixth

Steady funding, but to what end?

All figures in millions

	Earthquake prediction	Volcano prediction
1986	¥ 5,339 (US\$40)	¥ 488 (US\$4)
1987	5,320	595
1988	5,701	620
1989	6,020	674
1990	6,192	731
1991	6,669	698
Total	¥ 35,241 (US\$261)	¥ 3,806 (US\$28)

community in Japan by arguing (*Nature*, **352**, 275; 1991) that earthquake prediction is beyond the present capabilities of science and that Japan's earthquake prediction programme should undergo thorough external review. Following Geller's comments, many Japanese scientists have started to criticise the present system openly. The most recent is Seiya Uyeda, a professor of both Tokai University and Texas A & M University in the United States.

Vulcanologists seek to understand processes

Tokyo

ALTHOUGH Japan's earthquake prediction programme may not have much chance of undergoing significant change (see above), the same is not true for efforts to modify the study of volcanic eruptions.

One difference is that the chairman of the review committee of the volcanic prediction programme, Yoshiaki Ida of the Earthquake Research Institute of Tokyo University, is comparatively young and has strong views about where the field should be headed. He would like to see less emphasis on the empirical collection of data, and more effort spent on trying to understand the basic processes of volcanic eruption. That might include a search for magma chambers and the migration of magma using seismic techniques, as well as modelling such processes. Such an understanding, he believes, could mean a much more systematic approach to prediction rather than the

present way of "just trying to get precursors without physical reason".

Ida would also like to see Japan's vulcanologists spend more time communicating with the public. Japan's volcanic prediction committee has come under severe public criticism in recent years for its terse, uninformative and sometimes misleading statements about volcanic eruptions (*Nature* **351**, 511; 1991). In contrast, Ida says, the Philippine government preceded last year's eruption of the Pinatubo volcano by distributing videos showing the dangers of pyroclastic flows. It also issued public warnings, of increasing severity, in the weeks leading up to the actual eruption.

Ida says he does not expect "drastic" change in Japan's volcanic eruption prediction programme because his review committee is "rather conservative". But he does see hope for a "better trend".

D.S.

Italians first to use stem cells

five-year phase. It is this draft, not the deliberations of the science council panel, that will form the basis of government decisions about the next five-year plan. That plan would go into effect in two years.

The drafting committee was appointed by the earthquake prediction subcommittee of the Geodetic Council of Japan, an advisory body to the Ministry of Education, Science and Culture (MESC). Some senior scientists, such as Harumi Aoki of Nagoya University, are members of both groups. And these same senior people will examine the draft and make recommendations to the government this summer in time for the budget requests for fiscal year 1993, which begins next April.

This leaves the new Science Council subcommittee "powerless", says Geller. Geller and other critics have not even been shown the drafting committee's report, and there are no plans for them to see it. Tomowo Hirasawa of Tohoku University, who is chairman of both the new subcommittee and the drafting committee, says the views of the new subcommittee will be conveyed to the MESC earthquake prediction subcommittee by "individual members", in other words, by the same people who drafted the review.

The contents of the draft review remain secret. But Hirasawa says he thinks the present system of collecting vast amounts of data for empirical prediction is "basically correct". Geller expects the report to preserve the status quo. "No doubt the seventh five-year plan will be the same as the sixth five-year plan, which was the same as the preceding five plans", he says.

The Japanese situation stands in stark contrast to that in the United States, where hundreds of scientists, engineers, and government planners participated in a recent review of the US Geological Survey (USGS) earthquake hazard reduction programme. "Ten to fifteen years ago, US researchers put a lot of effort into an empirical approach to earthquake prediction just like Japan", says Hiroo Kanamori, director of the seismological laboratory at the California Institute of Technology in Pasadena. But current emphasis is on understanding the basic mechanisms of earthquakes and on research related to disaster mitigation.

In an effort to open the process slightly, the draft review of Japan's programme is being sent for the first time to six 'outside' reviewers, including the heads of the seismological and volcanological societies of Japan, and Masuo Iida, a former MESC official, who has been very critical of the present programme. However, the reviewers will have only a few weeks to comment on the draft report before it is submitted to the government in July, and substantial changes cannot be expected. And the people who chose these reviewers are the same people who set up the drafting committee.

David Swinbanks

London

AN Italian research group last week performed the first human gene transfer involving stem cells in the hope of curing a 5-year-old child with a rare genetic disease.

The treatment extends the work of Michael Blaese and French Anderson of the US National Institutes of Health (NIH), who since 1990 have used circulating lymphocytes to treat



Bordignon leads the way

two patients with adenosine deaminase (ADA) deficiency. The US scientists removed the patient's lymphocytes, transfected them with the ADA gene and reinjected them into the patients. But lymphocytes live for only a few months, whereas stem cells in theory have an unlimited life span.

ADA deficiency is a fatal disease that, at present, can be treated with conjugated bovine ADA or, occasionally, with bone-marrow transplantation. It is extremely rare, a fact that has hindered the use of such new genetic therapy techniques.

The Italian team, led by Claudio Bordignon of the H San Raffaele Research Institute in Milan, received permission in December 1990 from both its institutional ethics committee and the Italian Committee for Biosafety. Its approach is based on the original NIH protocol submitted by Blaese and Anderson, but modified slightly to include manipulation of the cells by a modified retrovirus.

However, a similar protocol from the US group has drawn criticism. After the recent approval by the NIH's Recombinant DNA Advisory Committee (RAC), members of the RAC's human gene therapy subcommittee, which was not consulted, questioned whether the accepted procedure for approval was followed, and worried that retroviruses not fully tested would be introduced into humans. However, the Italian committees were satisfied that Bordignon's amendment did not significantly change the original proposal for lymphocyte manipulation which had been approved in 1990 after extensive review by the NIH and the Food and Drug Administration (FDA).

Bordignon says that his work with paediatrician Alberto Ugazio is an important step forward for gene therapy, both ethically and clinically. First, there is a chance that the graft will take and the child will be completely cured. Second, the technique

makes possible consideration of important questions concerning the long-term survival of both lymphocytes and stem cells. By using two very similar vectors (differing only in one base pair) to transfer the ADA gene into peripheral lymphocytes or into stem cells, the scientists will be able to monitor circulating ADA-positive lymphocytes and determine whether they derived from stem cells.

The new protocol from Blaese and Anderson, which was reviewed in January, was considered to be an amendment to their original proposal, rather than a new proposal (*Nature* 346, 402; 1990). For this reason, the RAC chose not to consult its human gene therapy subcommittee.

Blaese and Anderson want to obtain stem cells from the very low levels circulating in the blood to avoid bone marrow sampling. They plan to prestimulate patients with granulocyte-colony stimulating factor (G-CSF) to increase their abundance. They now await clearance from the FDA and, ultimately, the NIH director.

Like the Italians, they will be using a modified version of their original virus to transfect stem cells so that the origin of surviving ADA-positive cells can be monitored. Dusty Miller of the Fred Hutchinson Cancer Research Center in Seattle, a member of the gene therapy subcommittee with expertise in vectors, believes that the RAC was wrong not to treat the protocol, with the modified as well as the original virus, as new.

"It is no trivial matter to say that using a new retrovirus is okay, just because retroviruses have been used before" says Miller. In other cases, the subcommittee has blocked approval for protocols where the investigator had unknowingly included an oncogene in the viral packaging.

Miller agrees that the Italian protocol poses no extra risk to the patient. But that is no justification for trying to bypass established routes for protocol approval and introducing undue elements of risk into early clinical trials, he says.

Both the American and Italian strategies for transfecting stem cells are simple adaptations of those used for lymphocytes. By contrast, a Dutch research group headed by Dinko Valerio received approval on 20 February for bone-marrow gene therapy based on an entirely different protocol (*Nature* 355, 190; 1992). It would allow them to condition patients fully to receive transformed stem cells from their bone marrow. Valerio says their data from long-term studies on rhesus monkeys have demonstrated the persistence of ADA-positive cells from all haematopoietic lineages. But the group has not yet gone ahead with its trial because there are no ADA patients in Holland.

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