

The long war against flu

That the H5N1 strain of bird flu has not yet caused a pandemic is no cause for complacency. Preparations for the inevitable must be redoubled to mitigate the potential devastation.

Five years after the deadly H5N1 avian influenza virus exploded into a global epidemic in birds, it has infected more than 300 people. Happily, it has not yet evolved into a strain that can transmit easily between humans — an event that would trigger a pandemic that could kill tens of millions. But as long as H5N1 continues to be present in animals, that risk persists. And with so many other flu strains out in the world, all constantly evolving, a flu pandemic is inevitable.

This grim reality has spurred basic research into topics such as the 1918 flu virus, cell-receptor biology and evolutionary dynamics, which are collectively yielding insights into the molecular basis of virulence and how viruses adapt to humans. Researchers have also begun to unravel the often fatal clinical events caused by the virus, such as the massive immune response that is a 'cytokine storm', and cell-culture technology is promising to make vaccines available more quickly. Plans by the Bill & Melinda Gates Foundation, the Wellcome Trust and the Pasteur Institute to roadmap this research should help focus priorities for funding, just as similar work has done for neglected diseases.

But improved control measures, especially for H5N1 itself, and public-health infrastructure are our frontline defences against a pandemic. Unfortunately, the overall control picture is bleak. Thailand, Vietnam and China have notched up successes in curbing outbreaks in birds, which is key to minimizing the chance that the virus can pass to humans. But South Korea had its worst outbreak ever in April, and the disease has become endemic in Indonesia, Bangladesh, Vietnam and Egypt. Eradication now seems impossible, and the task of containing the virus has become chronic and costly.

Many countries have made patchy progress in planning how to mitigate a pandemic once it does break out. True, any such plan can only buy time, by using antiviral drugs and restricting movement, until a vaccine is available for the specific strain that has broken out. The Commentary on page 162 endorses what might be an intriguing adjunct: 'pre-pandemic' vaccines, which would be matched not to

the exact pandemic strain, but to earlier variants. Even if these vaccines were only partly effective, advocates argue, they might confer sufficient protection to prevent death or severe disease. Although this idea is untested, it merits consideration — especially as strain-specific vaccines would be available only several months into the pandemic, and even then would be in very short supply. The World Health Organization is planning to stockpile more than 100 million doses of pre-pandemic vaccines, and some nations, including Japan, are considering the same.

But delivering sufficient perfectly matched pandemic vaccine fast enough to make a difference is the critical issue. One promising approach — equipping vaccines with adjuvants that boost their effect, reducing the amount of antigen needed in each dose — is belatedly getting the attention it deserves. Indeed, research is generating vaccine formulations that need so little antigen that timely doses could, in principle, be provided for everyone on Earth using existing plant capacity.

Rapid delivery will require an unprecedented level of international coordination. Plans should be in place so that when a pandemic strikes clinical trials of the strain-specific vaccine begin — as do the manufacture and distribution of the billions of syringes needed to deliver it. There should also be international mechanisms to ensure that developing countries have access to pandemic and pre-pandemic vaccines at low cost.

Surveillance, control of disease in animals, pandemic planning and vaccines — each requires intense, organized and sustained commitment. Even if H5N1 never evolves into a pandemic strain, it serves as a useful wake-up call, revealing just how much more must be done to be better prepared for the inevitable. ■

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An unnecessary battle

Neuroscientists and geneticists don't need to be at loggerheads over the biology of mental disorders.

Mental disorders take a staggering health and economic toll. The World Health Organization has estimated that unipolar depressive disorder alone is one of the leading causes of disability worldwide. Schizophrenia, bipolar disorder, autism and the many other psychiatric disorders only add to the misery. Yet progress in understanding the underlying causes of these conditions seems to be moving at a crawl. Genes are surely involved, but decades of futile hunting have made it painfully

clear that the contribution of any single gene to disease is probably minuscule.

How to find these tenuous connections is a contentious scientific debate, with geneticists and neuroscientists at an apparent impasse (see page 154). These two communities must start working together more constructively if they are to crack this challenging problem and ensure that the millions of dollars now flooding into this field are not misspent.

Many geneticists believe that scanning the entire genomes of a massive number of patients will uncover weak gene candidates by sheer statistical power. Yet some neuroscientists dismiss these studies, questioning the utility of indiscriminately seeking a swath of genes that are weakly associated with a condition, and that are unlikely to have relevance to its biology. Another concern is that diagnoses of psychiatric