and rational approach to the use of antivirals in a pandemic has yet to be determined. Hospital doctors will, quite reasonably, expect to have available antivirals to treat those requiring hospitalisation, although it will be impossible to know ahead of time whether they will be effective at later stages in a patient's illness. Some countries are planning to have national stockpiles. However, simply having a stockpile is not enough, and if one European country has a stockpile ten times larger than its neighbour, it cannot be therefore judged to be ten times better prepared. Since in order to be effective in treatment of influenza, antivirals must be delivered within 48 if not 12 hours of symptom onset, it can be seen that mass delivery to populations will be a major issue. A stockpile without a rapid delivery system will provide little protection. Some have proposed that there be a European Union stockpile of antivirals. A modest European stockpile could for example assist in protecting workers during poultry outbreaks close to Europe[1,2]. It would also be an asset in the unlikely event that the next pandemic started in or near Europe, so that WHO's stamping out tactic could at least be attempted, supposing the existence of a practical plan to do so [12]. However, rapid development and production of a pandemic vaccine will probably be more important for the second wave, with the more distant hope of more cross-protective vaccines that would protect against pandemic first waves (so-called universal vaccines) [13]. Equally important and more immediately accessible will be the simple public health measures (early self-isolation of those with symptoms, handwashing, respiratory hygiene, etc.) that are already available, and will save lives [14].

Is Europe prepared for a pandemic?

Not as prepared as it could or should be. Six national assessments have been undertaken by countries using a standard assessment tool and working with teams from ECDC, the European Commission and WHO European Region. These assessments (which will continue in 2006) found that while all six countries were preparing rapidly, all also had considerable way yet to go. Major issues remain to be addressed, notably the need for preparations to extend outside the health sector alone and for plans to be made more operational [15].

In conclusion, the threat from a pandemic has not been exaggerated. It could happen in 2006 from H5N1, or, more likely, in the future, and with another strain. However, in 2005 most European authorities and politicians started to give the risks the serious attention they deserve, and to invest the necessary resources to develop countermeasures. It is to be hoped that as the media interest inevitably declines, those in authority will sustain the investment and the levels of preparatory activity. Certainly, the pandemic risk will not decline.

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EDITORIAL

RABIES REMAINS A 'NEGLECTED DISEASE'

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Europe continually encounters the serious threat posed from zoonotic diseases including ancient bacterial agents such as *Mycobacterium tuberculosis*. The largest threat, however, is from RNA viruses such as the SARS-CoV, the Heninipah viruses, avian influenza viruses and emerging lyssaviruses. The ability of RNA viruses to expand their cell tropism in response to immune selection and to fill new ecological niches has demonstrated that this collection of viruses is extremely versatile with an enhanced capability for crossing the species barrier. One explanation that might account for this observation is that much higher nucleotide substitution rates for RNA viruses permit more rapid adaptation, greatly increasing the chances of successfully invading a new host population [1]. RNA viruses do not exist in a 'genetic stasis' and by mutation, crossing the species barrier, immune evasion and viral adaptation to a new animal host, further RNA viruses will emerge as human pathogens in the future and cause a threat to both animal welfare and human health in Europe.

The subsequent emergence of animal diseases that have the capability of crossing the 'species barrier' to humans ('zoonotic pathogens') will therefore continue to have a major impact on policy issues that relate to human healthcare. This has been witnessed with the re-emergence of rabies in some regions of Europe that were previously designated 'rabies-free', which has demonstrated the need for continual vigilance and the adoption of strict control measures. Despite the significant advances that have been made during the 20th century in reducing the burden of rabies, especially in central and eastern Europe, the disease remains endemic in many countries, largely as a result of financial limitations and a poor medical / veterinary infrastructure. Rabies therefore, remains a 'neglected' disease.

Since 1939, the epizootic of terrestrial rabies in Europe had spread 1400 km westward from Poland. It had been reported that the front of the epizootic advanced 20 km - 60 km per year [2]. Although other susceptible species, both wild and domestic, were involved in the epizootic, the red fox (*Vulpes vulpes*) was the principal reservoir, playing a key role in the maintenance and transmission of the virus. However, maintaining a rabies-free status, as reported by Servas and colleagues, incurs considerable costs and there is a continual risk of re-importation [3]. In France, Pr. Toma reports the effective reduction of rabies in the red fox [4]; however, the risk from rabies in imported dogs has since become a principal concern [3].

Since 1989, the increased use of oral rabies vaccines (ORV) has been instrumental in successfully eliminating sylvatic rabies from large areas within Europe. From 1990 onwards, we have witnessed the elimination of rabies from terrestrial mammals (principally the red fox) in many Western

European countries: the Netherlands (1991), Switzerland (1999), France (2000), Belgium and Luxembourg (2001) and the Czech Republic (2004) resulting in these countries being declared 'rabies-free'. Oral rabies vaccination (ORV) field trials were first reported in Switzerland in 1978 using a live-attenuated rabies virus strain (Street Alabama Dufferin, SAD). The use of a genetically modified vaccine (vaccinia recombinant expressing the rabies virus glycoprotein; VRG) has also been widely used in recent years. A planned and managed rabies control protocol with the use of ORV in urban areas complemented with intensified rabies surveillance has been proposed by Mueller and colleagues to tackle a residual focus of rabies in parts of Germany in the border triangle of Hessen, Baden-Württemberg and Rhineland Palatinate [5]. The results from the German study are very encouraging, with an obvious decrease in rabies incidence in the infected areas leading to the overall goal that Germany will be free of terrestrial rabies in due course. It is good to hear that the 'lessons learned' in reducing the incidence of rabies in western Europe can be applied to other rabies-endemic countries.

Moreover, elimination of rabies from the animal reservoir constitutes an investment in preventing rabies in humans. More recently, the Pan American Health Organisation has demonstrated that a reduction of canine rabies has correlated with a substantial decrease in human rabies cases. If rabies, as in the majority of Europe, is eliminated from domestic animals and wildlife, the incidence of rabies in man will also be controlled [6]. While the success of ORV in wildlife in Poland has resulted in a decrease in reported animal rabies cases, Sadkowska-Todys [7] and colleagues have not observed the expected reduction in the use of post-exposure prophylaxis (PEP) for rabies in humans. One possible explanation is that while rabies still circulates in animal reservoirs in Poland, any exposure, especially a biting incident is treated as a 'suspect' exposure, particularly if the animal carcass is not available for diagnostic testing. As rabies continues to remain a 'neglected' disease, an increased awareness of human infection is required, especially among the medical community, to ensure that PEP is administered in a timely and correct manner. This lesson was exemplified in the United Kingdom when a thirty seven year old woman died of rabies three and a half months after returning from a holiday in Goa, India, where she had bitten by a dog [8]. In this case, PEP was not administered. In 2004, the case of rabies in a 23 year old Austrian man after being bitten by a dog in Morocco as reported by Strauss and colleagues [9] further confirms the need to maintain awareness of the risks of rabies during foreign travel and to re-emphasise the public health challenge of 'neglected' diseases [10].

Another case of human rabies was reported in 2004, although at the time of death, rabies was not considered as the cause [11]. Following the death of the patient, various organs were transplanted into six recipients. Within six weeks of transplantation, three of the organ recipients developed encephalitis and died. Rabies was confirmed by laboratory diagnosis as the cause of death. The patient who received the liver was given immediate PEP and survived. The two recipients of the corneas were also treated and the grafts removed. Retrospectively, rabies was diagnosed in the donor from fixed brain samples and a history of a dog bite confirmed during a visit to India in October 2004. This incident followed a similar case in the United States earlier in 2004 [12]. The rabies transplant cases remind us to suspect rabies in unusual presentations of the disease. In addition, individuals with neurological sequelae and a history of travel to rabies-endemic countries should not be considered as suitable candidates for organ donation.

While the threat in Europe from rabies in foxes has diminished in western Europe as reported by Bourhy and colleagues [13], dog rabies in some eastern European countries, fox rabies in central and eastern Europe and racoon dog rabies in northeastern Europe continue to pose a risk. Moreover, Stantic-Pavlinic [14] reports that bat variants of rabies virus are an increasing threat throughout Europe, which has led to international organisations adopting the legislation that rabies variants in bats are now considered a statutory notifiable disease. European variants of rabies virus include the European Bat Lyssaviruses (EBLVs) types-1 and -2 (genotypes 5 and 6 respectively) [15,16]. Due to the protected status of bats in Europe, our knowledge of EBLV prevalence and epidemiology is limited. It is possible that EBLV is under-reported and that the recorded cases of EBLV represent only a very small proportion of the actual number of infected bats. Four additional lyssaviruses have also been isolated from bats in Eurasia (Aravan virus, Khujand virus, Irkut virus and West Caucasian Bat Virus) and have been proposed as new members of the *Lyssavirus genus*. Concerns exist that conventional biologicals will be ineffective against these newly emerging lyssaviruses and they will therefore have considerable public health implications [17]. Research is still required to further understand the role that insectivorous bats play in the virus-host relationship and subsequent transmission of EBLVs [18]. It is possible that insectivorous bats may harbour EBLVs for extended periods of time while the bat shows no obvious clinical signs ('silent infection'). Although it is feasible that EBLVs remain in the host in a 'latent' (dormant) state for long periods of time with potential 'asymptomatic carriage', strains of rabies virus are not, in general, considered to be 'persistent' viruses.

As the list of European countries that have eliminated terrestrial rabies continues to increase, the major issues will be on maintaining this situation. While the control of rabies in foxes is applauded, the vigilance and surveillance of rabies must continue especially in new reservoir species such as the racoon dog and in assessing the prevalence of new and emerging variants of rabies virus in European species of bats. This can be achieved through harmonisation of a laboratory network throughout Europe and in closer working between international organisations including the European Union, the Office International des Epizooties (World Organisation for Animal Health) and the World Health Organization.

Surveillance of rabies must continue especially in new reservoir species and in assessing the prevalence of emerging variants of rabies virus in European species of bats

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