five years. Some patients and their doctors desperately seek radical surgery as their only hope, but others have doubts about the evidence.[11] A trial is needed, and a pilot feasibility study (the mesothelioma and radical surgery "MARS" trial, funded by Cancer Research UK) is now under way. To answer the question 670 patients will be required over three years with five years' follow up. If achieved this would give an answer by about 2012 in time for the peak of the epidemic.

Irrespective of whether radical surgery will be considered much needs to be done in the care of these patients. The diagnosis should be made early and efficiently. Without it we cannot have meaningful discussions with the patient or plan treatment, and the patient's legal position in terms of compensation remains unclear. At the same time we try to control any pleural effusion to maintain breathing as long as possible.[6] This is best done by thoracoscopic talc pleurodesis, which can usefully be combined with surgical biopsy. Then with the diagnosis made the disease can be staged. If the pathological stage is early extrapleural pneumonectomy should be considered, and we would recommend that this is done in the context of multimodality treatment and within a study.[11] If the tumour is inoperable management can be with chemotherapy, and again it would be preferable that this is within a study.[12]

This disease is increasing in frequency. There is nothing we can do now to prevent it in workers exposed to asbestos throughout the 1950s, 1960s, and 1970s. What we can do is recognise it early, treat it actively, and learn about best treatment with carefully thought out studies because we will be seeing many more mesotheliomas in the next 25 years. In the developed world alone 100 000 people alive now will die from it.

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Pandemic risks from bird flu

The risk to humans is small, but we need to be better prepared

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An outbreak of avian influenza is ravaging the poultry industry in South East Asia. This carries a devastating economic toll for the communities affected, but what of the associated risk to human health? At least seven people in Vietnam have been infected by the strain of H5N1 subtype influenza found in poultry. Of these six are dead. In Thailand three boys contracted the virus; two are dead. These numbers are small, and investigations and case studies so far suggest that the virus does not transmit from human to human but is acquired directly from close contact with infected chickens. How likely is it that these events signify the emergence of a new human pandemic, and what measures do we have to deal with the global threat?

Although we think of influenza as a human disease, the natural reservoir for influenza A viruses is aquatic birds and wildfowl. Many different strains circulate at any one time, and most are not associated with disease in wild birds. Influenza strains are divided into subtypes depending on the antigenic nature of the H (haemagglutinin) and N (neuraminidase enzyme) proteins. A limited subset of influenza subtypes H1N1, H3N2, and H1N2 cause annual epidemics in humans, but all had their origins in avian species. They adapted for transmission in people following zoonotic events. Influenza virus has several options for creating genetic diversity. Firstly, it can shuffle genetic material derived from two different virus sources in an event known as reassortment. This was certainly the origin of the influenza pandemic strains of 1957 and 1968. Secondly, being composed of ribonucleic acid rather than deoxyribonucleic acid, influenza virus is error prone. Stepwise single mutations accumulate, and these can eventually alter the properties of the virus. This happened early after the H3N2 virus was introduced into the human population in 1968. Some changes occurred during replication of avian viruses in people during zoonotic events in Hong Kong in 1997, where six of 18 infected individuals died,[1] and in the fatal case of a veterinarian infected during a poultry epidemic of H7N7 influenza in the Netherlands last year, although these changes were luckily not sufficient to allow transmission between people.

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The virulence of the current H5 influenza strains is worrying. Although there is no evidence for virus replication outside the human respiratory tract, molecular properties—which lead to systemic disease in birds, leading to the name fowl plague—also correlate with lethality in mice[1] and possibly with the severe outcome of human infections. These viruses may also trigger inappropriate innate immune responses in humans, leading to severe respiratory disease and multisystem failure.[2 3]

Since H5 viruses have not circulated previously, the entire human population is naive and the severity of disease will not be tempered by any pre-existing immunity. The latter point is the greatest concern. If a new influenza subtype emerges in humans, mass vaccination would be the foundation of any control plan. Experience of generating vaccines against new subtypes is limited despite more than 40 years of experience of administering inactivated vaccines for human influenza. Traditional influenza vaccines are reassortant viruses, which have been shuffled artificially in the laboratory so that they contain the H and N proteins of the infecting strain. They are then amplified in eggs. Egg supplies may be a limiting factor in vaccinating large populations, but vaccines produced in tissue culture cell lines are still under development. Generating reassortants is time consuming and unpredictable. A newer technique allows genetic engineering of strains containing the correct prescription of genes, but no vaccines of this sort have been used in humans yet. The technical and regulatory hurdles to be overcome in generating an H5 vaccine cannot be underestimated.

Preventing the random events that lead to adaptive mutation or reassortment is the key to current control measures in South East Asia such as mass culls. The mobile wildfowl natural reservoir of influenza will never be eliminated, but depopulation of commercial poultry and improved hygiene will reduce the risk of zoonotic transmissions. Another approach is to vaccinate poultry, which has been successful in Mexico. Making poultry vaccines may be less problematic than generating human vaccines. Most importantly, people involved in the culls must not be infected with a currently circulating human strain; appropriate protection must be provided to them.

Antiviral drugs may be an important tool in controlling early events in the emergence of new subtypes in the human population. Two types of drugs that target influenza are licensed —amantadine, and inhibitors of the neuraminidase enzyme. Amantadine is unhelpful for the current outbreak since the strains involved already harbour a mutation, making them resistant to the drug. Neuraminidase inhibitors are active against the avian types of N protein but are not stockpiled in any quantity appropriate for mass use. Governments may need to mobilise funding to establish stockpiles.

As the outbreak develops over the ensuing days and weeks it should become clear whether this virus will spread world wide. The danger signs will be seeing human to human transmission with any noteworthy frequency, and genetic changes becoming apparent in viruses isolated from infected people. Even in the event of yet another lucky escape, more measures must be taken to limit the amplification of viruses with pandemic potential in the wet markets around the world.[4]

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Exchanging health lessons globally

BMJ issue will focus on lessons rich countries can learn from poor ones

The link between expenditure on health and health outcomes is not straightforward. Despite burgeoning health budgets, few countries in the developed world can claim to be delivering universally high quality, equitable health care. Could they have something to learn from less developed countries, whose meagre resources have long ensured that cost effectiveness is a dominant consideration?

Certainly, massive health bureaucracies and well endowed research institutions do not have a monopoly on wisdom. Examples of industrialised countries adopting treatments and strategies that were developed or pioneered in developing countries range from oral rehydration therapy (which was developed and widely used in Bangladesh before its slow but now global uptake) to limited lists of essential medicines. The experience in low and medium income countries of introducing national policies based on restricted lists of cost effective, affordable medicines over two decades prompted Australia to follow suit in the 1990s, and such a move has been mooted as a solution to escalating costs of medicines in the United States.[1 2]

Identifying promising initiatives in health practice, policy, education, and development should not be difficult. The Global Health Research Policy Network, led by the Center for Global Development, a think tank based in Washington, is about to publish an evidence based list of 20 successful, large scale global health interventions (www.cgdev.org). Defining the reason for success is a lot harder. Emphasising this, Nancy

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