

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 mice¹ 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

Birdsell, an economist at the centre, called for more research into “why programmes succeed when they do” at the Global Forum On Health Research in December.

Hardest of all is to recognise the lessons learnt from success or failure, see their wider potential, and successfully adapt them to other healthcare settings. Among the many factors that influence any project, sound management, good leadership, and active community participation are likely to be important. Brazil, for example, has succeeded in reaching and sustaining very high childhood immunisation rates against nine diseases. The last indigenous case of measles was reported in 2000.³ Public support for vaccination campaigns has been strong; temporary shortages of vaccines in 1997 resulted in public protests. This is in sharp contrast to the situation in several developed countries, where intense media coverage of possible side effects of vaccines and failure to mobilise public support have contributed to falls in immunisation rates.

The reluctance of health professionals in developed countries to abandon established treatments in favour of simpler low cost options may be one of the many barriers to adopting practices pioneered in less developed countries. Kangaroo care—keeping very low birthweight infants upright on their mother’s chest in direct, skin to skin contact, marsupial style—may be an example. It was developed more than 20 years ago in Colombia in response to overcrowding and lack of resources in special care baby units. Further evidence is needed to confirm promising results of its effect on reducing infant mortality, but it seems to offer additional benefits to mothers.⁴

In November the *BMJ* will publish a theme issue on “learning from developing countries.” Its aim is to flag up innovative, cost effective health initiatives and interventions in developing countries, which have or show

clear promise of having useful lessons for health professionals, policy makers, and researchers in the developed world. It also hopes to draw attention to initiatives that may promote learning between developing countries and discuss what we can learn from interventions that have failed.

Original papers for this issue should reach us by the end of May. Authors should discuss the potential of their work for wider learning and adaptation, and suggest what further research is needed to explore this. We also welcome submissions for other sections in this issue. In an increasingly globalised world we have much to learn from each other.

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Advice to contributors is provided on bmj.com. Submissions should be made to <http://submit.bmj.com/> and the covering letter should make it clear that the article is intended for the “Learning from developing countries” theme issue.

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Implementing the European clinical trials directive

Discussions continue in the European Commission and the United Kingdom

The European Union’s clinical trials directive must be implemented in United Kingdom law by May 2004.¹ It is intended to simplify and harmonise the regulation of clinical trials across the European Union, thereby facilitating the internal market in medicinal products while protecting participants and public health. Yet some have expressed concern that it will actually impede and inhibit publicly funded clinical trials, a sector of research in which the United Kingdom has always been strong.²⁻⁴ What are the contentious issues, and where do matters now stand?

The Medicines and Healthcare products Regulatory Agency (MHRA) is the regulatory body responsible for drafting the UK legislation to be laid before parliament early in 2004. In preparation for this the agency consulted widely in February 2003 and provided advice and a helpline via its website (<http://medicines.mhra.gov.uk/ourwork/licensingmeds/types/clintrialdir.htm>).⁵ The main concerns elicited were around the role and responsibilities of the spon-

sor of the trial, the delay and cost imposed by additional bureaucracy, and new requirements for good clinical practice, pharmacovigilance, and good manufacturing practice standards for investigational medicinal products.^{6,7} A joint project has been set up by the Department of Health and the Medical Research Council to help trialists and the Medicines and Healthcare products Regulatory Agency by documenting current best practice in these areas and to provide advice on systems and approaches that will comply with the law while minimising unnecessary burdens.⁸

The directive defines a sponsor as “an individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial” and sets out the legal obligations of the sponsor. The model is clearly based on the industry context, where the company taking an innovative compound through its development programme is self evidently the sponsor. Non-commercial

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