THE ROYAL SOCIETY

The Academy of Medical Sciences

# Summary of oral evidence: Dr Douglas Fleming

**24 May 2006**

Dr Douglas Fleming OBE FMedSci is Director of the Royal College of General Practitioners (RCGP) Birmingham Research Unit (BRU). BRU is concerned with the surveillance of diseases as they present to general practitioners and is funded by the Department of Health.

Members of the working group present were: Sir John Skehel, Professor Glynis Breakwell, Professor Neil Ferguson, Dr John McCauley, Professor Karl Nicholson, Dr Geoffrey Schild and Professor Robin Weiss.

**Key points**

The BRU is responsible for the RCGP Weekly Returns Service (WRS), a network of 73 general practices, covering approximately 800,000 people, located throughout England and Wales that collect information on every consultation and new episode of illness diagnosed in general practice. Reports began in 1964 but data collection began in 1967. Respiratory tract infections are routinely reported on a twice-weekly basis and practices who conduct influenza viral swabbing are also included.

The WRS is a unique database worldwide and includes data for the 1969-70 influenza pandemic in the UK. Even with this data it is still unclear why the pandemic hit the UK a year later than much of the rest of the world.

***Severity of epidemics/pandemics***

The database has shown that the number of persons presenting to GPs has not changed substantially over the last 40 years, but numbers consulting for acute influenza like illnesses are now much less than those seen in the 1960/70s. Recent influenza epidemics have been much less severe than those seen in the 1970s. Dr Fleming told the group that he believes recent influenza seasons have been less severe as they have been due to constant mutations in strains of H3 and there is now little naivety left amongst adults. However, he believes that we will return to illness levels reflecting more severe winter seasonal epidemics in the years immediately after the emergence of a pandemic strain. Furthermore we should be planning for successive years of increased influenza activity and not simply for a pandemic year. Dr Fleming believes that if an H5N1 pandemic occurs, the effects will be apparent over several winters and annual vaccination policies will need to take note of the likely increased demand. The notion of waves of a pandemic should preferably be thought of as waves of illness due to drifting variants of a new pandemic strain.

Dr Fleming presented data on the incidence of influenza over an 11 week period (the typical duration of an influenza epidemic) stratified by age. In 1969/70 it was the 45-64 age group which had the greatest incidence of influenza, but other epidemics had different patterns: for example in 1989 and 1993, children had the highest incidences. Dr Fleming told the group that in the winter of 1999/2000 flu like illness almost crippled the health service though he suspects that influenza was mixed with Respiratory Syncytial Virus (RSV). Children escaped severe levels of illness in this winter. Recent epidemics have mainly affected children and persons over 75 years. Persons over 75 years are now significantly worse hit than those aged 65-74 who perhaps should now be considered a comparatively healthy population.

Excess mortality due to influenza was largely confined to the oldest age groups (especially over 75 years) and estimates of excess hospital admissions due to respiratory disease were similarly restricted to the elderly but it was particularly relevant to note that these estimates were not much less now than in the 1969/70 pandemic

suggesting that at least in this age group the impact of increased vaccination against flu was not as effective as some thought.

***Virological investigation and diagnostic tests***

Virological investigation of patients diagnosed in the WRS sentinel practice network is done by the Health Protection Agency centrally in Colindale and Dr Fleming believes that this service needs more money to be invested in it.

Dr Fleming was asked about rapid 'bedside' diagnostic tests for influenza. He told the group that they take at least 10-15 minutes which is longer than the average GP/nurse consultation. He believes that the tests that exist are good but they will need to be of the quality and speed of urine dip stick tests before they will be used routinely, even on a limited basis.

Dr Fleming told the group that he doesn't think the tests are needed in general practice, although they could be used for anonymised surveillance in sentinel practices, but they don't provide a sample of the virus for routine typing (unlike current virological investigation). The tests are not cheap and the cost is more than double that of a dose of Tamiflu. However, he believes that there may be a role for the tests in selected settings such as in a hospital especially for recognition of infection in front line healthcare staff in the early phases of an epidemic. Professor Nicholson told the group about a project he has just begun looking at rapid tests in an elderly population. All the test results which came back positive by using PCR all came out negative using any of the rapid tests available on the market.

***Policy making***

Dr Fleming was asked about current policy making and if the government could be better prepared. In particular, if there is evidence of efficacy of vaccinating groups who are not currently immunised. Dr Fleming told the group that recent trials for influenza vaccines and treatments have been conducted over the last 15 years when epidemics have been minor. In his opinion, if the trials had been done in the 1970s when the epidemics were more severe then the vaccines would have produced better results especially when considered in terms of cost effectiveness. Since most research work on interventions for influenza has been undertaken in the last 15 year period he believes that informed opinion becomes more important than evidence.

Dr Fleming told the group that vaccination is desirable and should be used in more groups as it is likely that we will return to the situation of more severe epidemics seen in the 1970s. But he is worried that vaccination is not working well in the age group over 75 as admissions to hospital related to influenza have remained constant even though the level of vaccination has increased. We have to look at different approaches to vaccinating persons over the age of 75 and perhaps not be restricted to the standard trivalent split virion vaccines. Certainly, policy decisions should not be exclusively based on evidence from the 1990s. We also need to recognise the accumulated knowledge and experience of doctors treating patients. Changes in demographics were discussed briefly. Elderly persons in home care are now admitted to hospital more often and the numbers of persons in the age group (especially of persons living alone) has increased.

Dr Fleming was asked if the information collected by the RCGP is used appropriately by Government and he told the group that data from the 1969 pandemic has been used by modellers to give a basis for pandemic planning.

***Treating a pandemic***

Dr Fleming was asked if there are any issues for primary and secondary care that need to be addressed to better prepare for a pandemic. In Dr Fleming's opinion, primary care services have been dismantled. To treat

any pandemic effectively, he believes that existing services should be reinforced and managed at a local level rather than trying to introduce new ones at a national level. He believes there is also an issue of the availability of intensive care beds in a pandemic. A telephone-based triage system could be introduced which would be better done locally with healthcare workers who know the community rather than anonymously at a national or regional level.

In 1969 the maximum rate of influenza cases was 1250 per 100,000, with an average of 780 over a four week period. These figures are high but the UK coped and Dr Fleming is convinced that the UK would be able to cope again in a similar situation. There are limits as to what might be considered a reasonable basis for planning and a 25% clinical infection rate spread over 8-12 weeks seemed reasonable.

***Antivirals***

Dr Fleming is concerned about the plans for the delivery of antivirals in a pandemic. The UK now has much of its stockpile of antivirals and should now plan for the delivery to those that need it. We are no longer in a planning scenario in which these drugs were not available. When asked about the availability of antivirals for 25% of the population, Dr Fleming told the group that the country probably couldn't cope with planning for much more than 25% of the population being infected in a pandemic.

Dr Fleming was involved in some of the clinical trials for Relenza. The trial he was involved with recruited individuals as they presented to GPs with influenza-like symptoms and the trial showed a benefit of 2.5 days after taking Relenza. In other trials, participants were recruited more generally (for example, at University campuses) and therefore may not have had influenza illness of a severity which might have prompted them to seek treatment directly. Most other trials only showed an improvement of 1- 1.5 days.

Dr Fleming told the group that in a pandemic, the virus may be more virulent and therefore replicating and shedding for longer. Therefore the neuraminidase inhibitors may be effective for longer than the recommended 48 hours after the onset of symptoms if replication is still occurring, perhaps up to three or four days. They may also have to be given for a longer period.

There was a discussion on the best time to give Tamiflu. Dr Fleming advised that it should be given as an early treatment for people who have been in contact with an infected individual. They should monitor their temperature and receive Tamiflu if their temperature increases. However, members of the working group suggested that this situation may lead to an increased likelihood of the development of resistance as the viral load is very high at that point. Nevertheless this was inevitably the time that most persons needing treatment would be receiving antivirals.

Dr Fleming believes that the issue of Tamiflu as a prophylactic treatment is not reasonable unless there is an effective vaccination waiting in the wings. However, Tamiflu could be used prophylatically for frontline medical staff.

***Pandemic vaccines***

Dr Fleming would not encourage a stockpile of pandemic vaccine, but was asked about using a current H5 vaccine as a priming dose. He said that evidence would be needed to justify the policy, although only small experiments would be needed. However this would be a very large step in policy terms.

He was asked if a poorly matched vaccine which could be stockpiled in advance would be protective. From the RCGP data it can be shown retrospectively that in recent years when there was not an exact match of the virus strain used for vaccine production there was a recognisable increase in morbidity.