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EDITORIAL

Get political: the case for greater virological leadership

The Western world may be showing a progressive loss of self-confidence and initiative, but in matters virological, this is being compensated for by the growing research productivity of post-Soviet Eastern Europe, South and South East Asia and South America. These regions are now all prolific sources of clinical virological discovery and innovation.

Across this expanding research base, though, English continues to be the language of scientific discourse, and its dominance remains as an advantage to native and other fluent English speakers. It is an advantage which carries obligations with it, however. One is the responsibility that virologists with an easy command of English should feel both in assisting in preparing original work for publication and in taking a large share in the process of editing and peer reviewing for English language journals. Another obligation is for them to bring their knowledge and experience to the decision-making table and to strive to explain what virology can and cannot deliver. Leaving policy-making and resource prioritisation to non-virologists may make for a quieter life; but in the fields of public and veterinary health in particular, the consequences of virologists not involving themselves are likely to be poor decision-making, wasted resources and missed opportunities.

Recent examples show what happens when orthodox virological opinion has not been sought or has been ignored. Take the prediction of influenza outbreaks, an area where even experienced virologists fear to tread. If the field is left entirely to vested scientific interests, commercial agendas and panicked politicians, stock piling of hastily manufactured vaccines for epidemics that do not materialise is almost inevitable. In 2009, the perceived threat of a major influenza pandemic also led in several countries to disproportionate governmental purchases of an antiviral agent, oseltamivir ('tamiflu'). Quantities of that drug are now sitting unused in stores, dispensaries and bathroom cabinets [1]. This happened not only because the pandemic was far less severe than feared but also because virological voices were not raised to remind advisory committees that antivirals have narrow windows when used for prophylactic and therapeutic purposes against acute infections. Had the indications for using tamiflu been properly defined, less would have been procured in the first place. Instead, family practitioners and even lay people were given access to a novel drug without being told when it was, and when it was not, likely to be effective. Consequently, most of the small proportion of the stock pile that was used was probably taken inappropriately. Next time, it is to be hoped that things will be better managed. Unfortunately, though, damage has been done to the reputation of tamiflu and perhaps of antiviral drugs in general.

At the end of the1990s, a small group of authors from a virologically naive department in a university hospital in London gained currency for their theory that measles, mumps and rubella (MMR) vaccine gave rise to serious side effects [2]. The immediate outcome was a reprise of what had already happened in the UK 20 years before when a lone British academic called into question the safety of a well-tried whooping cough vaccine [3]. As a result, acceptance rates for it plummeted. Similarly, what turned out to be a groundless MMR vaccine scare [4] caused acceptance rates to fall sharply, and they have not yet fully recovered. As well as MMR vaccine not being given, the scare also led to the irrational expedient of giving the measles component of the vaccine separately. Some virologists muttered feeble reservations about any linkage of MMR immunisation with side effects like autism and the implausibility of attenuated virus strains doing what wild virus strains were not known to do; but this should have been pointed out plainly at the outset. Instead, virologists failed to challenge the original paper in the reputable journal that had published it, and a generation of unimmunised young adults has emerged since then, many of whom find themselves susceptible to one or more of the diseases in question.

These examples of the vulnerability of national childhood immunisation policies are drawn from the UK, but they have had a wider resonance just as those originating in other countries have done. In France, in the mid 1990s, the suggestion that hepatitis B vaccine induced an MS-like demyelinating disease in children has disrupted that immunisation [5]. In spite of the vaccine's excellent track record, a 'precautionary principle' immediately prevailed in France, and the issue has still not been settled. The USA, by contrast, has a better record. A weak association of the first candidate rotavirus vaccine with infant intussusception interrupted its use there, but after a prompt and painstaking review of the evidence, the vaccine was modified and confidence was restored. More acceptable rotavirus vaccines have since been introduced and widely used [6].

Orthodox virology can contribute in other areas than vaccinology. In 2001, a widespread outbreak of Foot and Mouth Disease (FMD) in the UK was dealt with by a ruthless cull of cattle, sheep and pigs. This followed a signal failure to control the movement of animals as soon as the outbreak came to light, which meant further dissemination of the infection. The eventual response to the delayed recognition of the outbreak, led from high up in Government, was a brutal and expensive FMD eradication campaign which in retrospect could have been pursued more moderately. Virologists exerted little or no influence on the policy, and the outbreak was only contained at inordinate cost.

The compensation and re-configuration that followed allowed the farming industry to recover from that epizootic, and whether or not the actions taken at the time were excessive what now matters is that current contingency plans against a future introduction of FMD are appropriate and kept updated by incorporating scientific advances. In particular, the routine use of real-time diagnostic PCR, not available to veterinarians in 2001, should now enable outbreaks even of diseases as infectious as FMD to be extinguished at an early stage.

Farmers in the UK and other parts of Western Europe are now being confronted with a midge-borne infection of ruminants, Schmallenberg virus. It seems to affect productivity and fertility, and in the fetus it causes limb malformations that impede parturition. Calls for a Schmallenberg vaccine are unlikely to be met within the short-term, and meanwhile husbandry may need to be modified so that tupped ewes are not exposed to midges at the critical time early in pregnancy. Virologists should give their attention to contingency planning against such disease outbreaks and think prospectively about how future comparable public health and veterinary issues might evolve and be dealt with.

There are other issues, often concerning the control of local outbreaks, that would benefit from more assertive virological input, for example, fully containing environmental exposure to vomit and faeces during institutional norovirus outbreaks, taking precautions to prevent transplant-related and other iatrogenic virus transmissions, and persuading healthcare workers to get themselves vaccinated against seasonal influenza (in the UK only about a third of them do so at present). But there are also national, regional and global issues for which it is crucial to ensure virological coherence if maximum benefit is to be gained. For instance, adherence to well established principles will make any immunisation programme more effective. HBV vaccine holds out the promise of eliminating that infection within two generations, but only if both horizontal and vertical transmission of the virus are targeted. Neither route is easy to interrupt, the vertical one the more so. In several developing countries where HBV is endemic, young children are now receiving vaccine. However, until prompt postnatal immunisation of the infants of maternal carriers is instituted worldwide, some mothers will continue to infect their children. This is a logistical challenge that even advanced countries have found it difficult to meet, but it has to be recognised as a necessary part of a fully successful prophylactic programme.

The application of best virological principles and practice needs not depend on the availability of unlimited resources: sometimes the opposite. Virologists can inject realism into an extravagant programme and uncover opportunities to improve cost-efficiency, both nationally and supra-nationally. The continuing national provision of containment level 4 (CL4) laboratory facilities for the occasional urgent diagnosis of importations of exotic and zoonotic viruses is a case in point. At the national level, this has often been beset with technical difficulty, high cost and the need for back-up sites. A strong case could now be made for the regionally based and funded provision of state of the art back-to-back facilities, for example, by the European Union. At

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such supra-national laboratories, a continuously available diagnostic capacity could be maintained together with a lively CL4 research programme.

The current goal of eradicating polioviruses and then discontinuing immunisation against them assumes the existence of a universal geo-political stability [7]; but this seems unlikely to prevail in the foreseeable future. Realism argues for a switch of emphasis from virus eradication to virtual disease elimination sustained long-term—that is, an achievable aim that will also allow cost-benefit ranking of polio alongside other global immunisation goals. The same holds true for global measles as for polio eradication. Disease elimination is highly desirable and is feasible in well-ordered states; but to argue for global measles eradication, as has recently triumphantly been achieved for rinderpest virus, is to assume that humans can be treated like cattle. In the past, a few states have done this to their subjects, but thankfully most of them no longer exist. So, admirable though global smallpox eradication was, it is a historical example that distorts the current prioritisation of available resources for global viral prophylaxis. There are virological and practical reasons why all other human viruses are likely to be much harder to eradicate than smallpox was.

The lack of an early prospect of a comprehensive HIV vaccine is disappointing, but it is mitigated by the good results of combined drug therapy. This has transformed prognosis and begun to suppress HIV transmission. In the particular case of mother–child exposure, it has long been known that drug prophylaxis can be effective; but in the context of sexual transmission, the potential of antiretroviral therapy to lower infectiousness is, especially with investigations of virus concentrations in the semen of treated men, now being acknowledged [8]. General virological principles and the sequential observation of individual infections have also led to a realisation that the initial viraemia of HIV infection is the peak viraemia, so that it is early diagnosis and prompt therapeutic intervention that will best interrupt virus spread. It also seems likely that early treatment will best preserve an individual's immune capacity long-term. Convenient oral antiviral drugs are now playing a leading part both in the treatment and the prevention of chronic viral infections such as HIV and hepatitis C [9,10], with beneficial prognostic and public health consequences. The initial costs are going to be high and long-term side effects will have to be considered; but virologists can help in developing rational policies for the use of these drugs just as bacteriologists have done for antibiotics. The suppression and elimination of harmful carrier states are major challenges for clinical virology. Others are, for instance, to determine the extent of the effect of intrauterine viral infections on pregnancy outcomes and the full range of opportunistic infections associated with the growing use of immunosuppressive therapies.

Broadly, the choice now before virologists is this: either to stay in the laboratory and leave policy making to politicians advised by less well informed colleagues, or to engage in the broader debate and take on more of the responsibility for decision making. Every branch of medical science has in its past giants on whose shoulders today's practitioners stand, and virology is no exception. Among those who laid the foundations of virological diagnostics, vaccinology and therapeutics were figures who, if alive today, would be articulating what our specialty can now offer to improve national and global health. These pioneers were not shrinking violets, nor did they run their laboratories as intellectual silos. To the extent that we, by contrast, are guilty of being or doing those things, I suggest it is the time to get back to the front line. The specialty has much to offer both to the individual patient and to the community, but it must seek to explain this in terms understandable to all. The aim should be to ensure that current virological knowledge and present endeavour brings the maximum benefit to as many people as possible.

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