

A young boy with short brown hair is shown in profile, covering his eyes with his hands. He is wearing a blue t-shirt. In the background, a woman with dark hair, wearing a light blue shirt, is looking towards the boy with a concerned expression. The setting appears to be a clinical or hospital environment.

# Vaccinations

## for non-infectious diseases

Daniel Ryan describes  
the recent developments.

**The use of vaccination in medical practice has a long and rich history, with Edward Jenner introducing the term in 1796 to describe the systematic use of cowpox (Latin – vacca) to inoculate individuals against highly virulent small pox. Since then vaccines have been developed for a whole succession of infectious diseases based on the concept of an initial controlled exposure to inactivated infective agents or component fragments, which produce an immune response that would protect the individual against future exposure.**

Children in the UK are routinely vaccinated against 12 different infectious diseases. However, the re-emergence of measles in many parts of the UK illustrates how confidence can be shaken in a vaccination process, with public concern over unsubstantiated claims of association between autism and the MMR (measles, mumps and rubella) triple vaccine driving a significant fall in the levels of inoculation.

### **Expanding roles for vaccination**

A number of biotechnology companies have considered the possibility of vaccination being used in the treatment of existing non-infectious disease, rather than just preventing infectious diseases, and more than 20 therapeutic vaccines have been tested over the last 12 years. Some of these vaccines target foreign molecules, such as NicVax from Nabi

Biopharmaceuticals for treating nicotine dependency. These vaccines conjugate virus-like particles that promote a strong immune response with derivatives of the target molecule. Nicotine, for example, is physically prevented from accessing target areas in the brain associated with relaxation and appetite suppression by antibodies binding to the molecule. Phase two clinical trials have indicated comparable smoker cessation rates at one year to the best current treatments, such as bupropion. However, future trials and evaluation are necessary before such a vaccine becomes a commercially available prospect.

Other vaccines provoke immune responses that block potentially damaging pathways in the body. Cytos Biotechnology and Protherics have both developed vaccines that target angiotensin, and have demonstrated reductions in blood pressure for those with hypertension. In 2003, Avant announced results from a phase two clinical trial on the cholesterol management vaccine, CETi-1, which boosts the concentration of HDL or 'good' cholesterol in the blood, whilst more recently, Bioinvent and Genentech are developing a vaccine that targets oxidised LDL or 'bad' cholesterol, which is instrumental in plaque formation in arterial walls.

The role of infectious disease in some cancers is also well-established. For example, certain strains of human papilloma virus (HPV) and hepatitis B and C virus have been implicated in cervical and liver cancers respectively. This has led to the implementation of a new vaccination programme against HPV for girls at age 12 in the UK.





However, more recent research has focused on cancer vaccines that restrict the growth of existing tumours or that act synergistically with other treatments to prevent recurrence.

The key difficulty for such cancer vaccines is that the immune system has evolved to identify very different organisms such as bacteria and viruses, whereas the differences between normal and cancerous cells are more subtle. Auto-immune diseases, such as rheumatoid arthritis, are the hallmarks of an immune system that is too active and intolerant. Cancer vaccines need to either identify unique cancer-related molecules that are rarely found on normal cells, improve the visibility of cancerous cells to the immune system or 'educate' key components, such as dendritic (immune) cells.

Patient compliance is a particular concern for the treatment of chronic disease, whether due to forgetfulness or reactions of patients to the diverse effects of the treatment. Vaccination could replace the need for daily or

more frequent tablets with periodic booster injections, as well as providing for significant cost savings in treatment administration. Vaccines would be expected to avoid the 'off-target' effects commonly seen with existing drugs, but may have unforeseen effects where the underlying processes and pathways that are affected by such vaccines are not fully understood.

### Implications

Despite the wealth of different strategies being researched for the use of vaccines in the treatment of non-infectious diseases, it should be remembered that as yet, there are no such vaccines available outside of clinical trials.

However, it is clear that the pace of development is increasing and some of these vaccines are likely to enter clinical practice over the next five to ten years. Cytos Biotechnology, for example, announced an agreement with Pfizer in August 2008 involving funding of CHF150 million (US\$140 million) for research and development. In return, Pfizer gained worldwide exclusive rights to any new vaccines that are based on the 'Immunodrug' technology of Cytos.

As insurers attempt to assess the effect of such vaccines, it is unlikely that cost will limit uptake in an insured population, even if national vaccination programmes are not implemented. The retail cost of the

recommended three doses of the recently developed HPV vaccine is £240. In contrast, the total cost of administering herceptin for early or late stage breast cancer over a recommended period of up to one year is £20,000. Potential improvements in morbidity and mortality could be significant given the tightly focused actions of the vaccine, for example, leading to significant improvements in smoking cessation or reductions in blood pressure to more optimal levels.

In practice, it is likely that the overall impact on any population will be much more subdued. If a significant minority of parents are unwilling to allow their children to be vaccinated against measles, is it reasonable to assume that the level of concern will be far greater when the targets of vaccination are only subtly different from normal cells and vital pathways. Individuals, after all, can always stop taking medication.

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