Vaccinating boys against HPV to reduce cancer rates across the sexes

In most countries, vaccines against human papilloma virus (HPV) are recommended only for girls in order to prevent cervical cancer caused by persistent HPV infection. However, there is increased evidence that HPV causes other forms of cancer, including throat, penile- and anal cancer, supporting the push of public health to vaccinate both boys and girls. Australia was the first country to implement HPV vaccination for boys earlier this year.

A Canadian study in the journal *Sexually Transmitted Infection* looked at data from 16 different studies involving more than 5000 people to analyze rates of HPV vaccine acceptability and examined what factors play a role when determining whether young men receive the vaccine. According to study lead author Dr Peter Newman from the University of Toronto, misinformation and unfounded vaccine fears can result in cancer deaths that could have been avoided with simple vaccination. Logistical barriers, such as out-of-pocket cost, transportation to a clinic and wait times for the vaccine, may also reduce the acceptance of new vaccines. One of the biggest factors affecting male HPV vaccination rates has been the lack of a well-established connection linking HPV in men to a life-threatening illness—as is the case for HPV and cervical cancer in women—however, it looks like this is changing.

A recent study published in the journal *PLoS ONE* suggests that GSK’s bivalent vaccine Cervarix (HPV16/18) can prevent some cases of throat cancer. The HPV vaccine was tested against a control vaccine in 5840 sexually active women between 18 and 25 years of age in Costa Rica. Four years after vaccination, HPV 16 or 18 was found in the throat of one of the women who received Cervarix. In the control group 15 women were infected. While the study has some weaknesses such as enrolling only women and taking only one oral sample, the study is strong enough to add solid evidence to the belief that HPV vaccines can prevent throat cancer.

Another recent article made the case for extending HPV vaccination to young gay men. In their Editorial in the journal *Sexually Transmitted Infections,* UK researchers report that the risk of developing anal cancer is 15 times higher in homosexual than in heterosexual men. They suggest that targeted vaccination would be cost effective for the National Health System. While rates of anal cancers are higher among men who are also HIV-positive—despite antiretroviral treatment—they are also higher among gay men who have not been infected with HIV, according to this paper. In Australia, HPV vaccination of girls was shown to have an impact on the prevalence of genital warts in heterosexual men, but no such change has been observed in gay men.

Finally, HPV has also recently been linked to esophageal cancer. According to an Australian study published in *PLoS ONE,* HPV infection triples the risk of people developing esophageal squamous cell carcinoma (OSCC). This form of cancer is usually diagnosed late in its clinical course and thus has a very high mortality. Worldwide it is the sixth highest cause of cancer-related deaths, being particularly prevalent in China, South Africa and Iran among men in their mid-70s to 80s. It is not known why prevalence in those countries is so high, but it is thought to be linked to dietary, lifestyle and environmental factors. Now that HPV has been identified as another factor causing OSCC, the idea of vaccinating boys against HPV could get a new spur, especially in countries where OSCC is frequently found.

In the recent past, HPV has been linked to a variety of cancers, including anal, penile and certain types of throat cancers in men, and the virus is also responsible for various cancers in women. Vaccinating boys will play a crucial role in reducing cancer rates across the sexes.

**References**

1. Newman PA, et al. *Sex Transm Infect* 2013; 89:568-74; PMID:23828943.
2. Herrero R, et al; CVT Vaccine Group. *PLoS One* 2013; 8:e68329; PMID:23873171; http://dx.doi.org/10.1371/journal.pone.0068329
3. Lawton MD, et al. *Sex Transm Infect* 2013; 89:342-3; PMID:23858494; http://dx.doi.org/10.1136/sxtrans-2013-051176
4. Liyanage SS, et al. *PLoS One* 2013; 8:e69238; PMID:23894436; http://dx.doi.org/10.1371/journal.pone.0069238

New melanoma vaccine contains natural product from marine sponges

A new melanoma vaccine will be tested in Wellington (New Zealand) on humans for the first time. The dendritic cell (DC)-based cancer vaccine contains a synthetic ingredient that is based on a natural product discovered in marine sponges ten years ago. After five years of research and $4.5 million for R&D, the vaccine is entering the clinic.

Manufacturing the vaccine has been a nationwide project involving Callaghan Innovation, Cancer Trials New Zealand and the University of Auckland. The vaccine is made from DCs, which are removed from a patient’s blood and mixed with synthetic protein fragments that are common to melanomas. A glycolipid called alpha-galactosylceramide is added—this is a synthetic version of a natural product found in a marine sponge. The vaccine will be kept in the laboratory for a few days before being injected into the patient.

Professor Ian Hermans from the Malaghan Institute of Medical Research in Wellington believes the synthetic ingredient, initially identified in sponges, will boost the immune system’s response to cancer by activating T cells in the blood to hunt and kill tumor cells.

“We have had chemotherapy and we have had radiotherapy and surgery, and they have all been useful and effective to some degree,” he said. “But there has not been a big new treatment modality for a long time, so that is why people are excited. I think the real excitement will be how we slot it into some of these existing treatments.”

The Phase 1 clinical trial will include around 40 subjects and is expected to take two years to complete. Participants will have to meet strict criteria including a history of successfully treated melanoma. Half of the trial patients...
will receive a potent version of the vaccine containing the marine sponge derivative, and half will receive a vaccine without it.

If clinical development of the vaccine is going well, it will be refined in the laboratory with the ultimate goal of creating a synthetic off-the-shelf version that does not involve taking cells from individual patients and mixing them with manufactured ingredients.

New Zealand has one of the highest rates of melanoma in the world, with about 300 deaths each year from the most aggressive type of skin cancer.

Impact of Hib conjugate vaccines in developing countries

According to a series of papers sponsored by GAVI Alliance and published recently in a Supplement of the Journal of Pediatrics (Volume 163, No 2, Aug 2013), the conjugate vaccine against *Haemophilus influenzae* type b (Hib) is having a large impact in developing countries. Over an eight-year period, more than hundred researchers in seven different countries investigated the impact of the Hib vaccine. They found that the vaccine has a significant impact on countries in Asia and Eastern Europe. In Mongolia for example, vaccine effectiveness is evident: cases of Hib meningitis decreased by 2010 from 28 to 2 per 100,000 children. Other countries, including Gambia and Mozambique, showed similar positive results. Another study also showed that the Hib vaccine was cost-effective in areas where the disease burden is higher and access to care is lower.

Before the widespread use of Hib vaccine, Hib was the most common cause of bacterial meningitis and a major factor in causing severe pneumonia in children under five years of age. Hib conjugate vaccines were introduced in developed countries in the early 1990s, resulting in a virtual elimination of the disease. In developing and low-income countries, the introduction of the vaccine was delayed due to multiple barriers. In 2005, the GAVI Alliance funded the Hib Initiative, a consortium of public and private institutions, to assist countries eligible for GAVI funding in making evidence-based decisions regarding the introduction of Hib vaccines into national immunization programs. Fortunately, significant progress in introduction of Hib vaccines has occurred over the last few years with all GAVI countries, and disease reduction can already be seen in some of the countries.

Electronic health records to keep track of immunization status

In a recent study, researchers from Columbia University, Weill Cornell Medical College looked at registry efficiency and Electronic Health Record (EHR)-based reporting. They found that using an EHR system to automate the immunization data shared between health providers and public health agencies enables physicians to assist individual patients faster and more effectively, while also providing more immediate, cohesive community data to the agencies tasked with promoting public health.

Automated reporting was also found to reduce the lag time historically associated with data submitted on vaccinations and, in some cases, reduced the paperwork and staff time traditionally devoted to managing these required submissions. In summary, a robust records automation program increased knowledge about both individuals and communities, allowing medical and public health officials at all levels to make more informed decisions. The study, recently published in the journal *Applied Clinical Informatics,* analyzed 1.7 million records submitted by 217 primary care practices to the NY Citywide Immunizations Registry between January 2007 and June 2011—both before and after the launch of automated reporting via an EHR. Differences in records submitted by day, by lag time, and by documentation of eligibility for subsidized vaccines were examined.

“The efficiency offered by automation has significant implications for managing public health, whether it is by informing a local physician on the health of an individual or informing policymakers on health trends within a whole community,” said lead researcher Dr Jacqueline Merrill from Columbia University. “For example, EHRs greatly enhance our ability to help at-risk populations for whom up-to-date immunizations are critical, such as children, immunosuppressed individuals, or the chronically ill. Before automated registries, reporting was less structured and data submittal was less consistent.”

In the US, health officials currently recommend immunization against 17 vaccine-preventable diseases. However, tracking vaccinations is difficult, especially among underserved populations whose care is often managed by multiple providers. Various state and local health agencies started to keep immunization registries to consolidate scattered patient records and thus reduce unnecessary vaccinations. However, registries frequently report slow and incomplete data submission by health providers, who in many areas still submit information via paper files. Automated reports via EHRs provide readily available immunization histories, which can help officials and providers determine which patients have been adequately immunized. Registries also track and provide the basis for decisions on vaccine formulations, vaccine supplies and delivery schedules.

“Automating the process appears very successful”, said Dr Merrill. “In fact, it is so successful that we believe it would be beneficial to retrofit data from the past so it can also be included in the EHR.”

Reference

5. Merrill J, et al. Appl Clin Inform 2013; 4:267-75; PMID:23874363; http://dx.doi.org/10.4338/ACI-2013-02-CR-0009
Pregnant women urged to get whooping cough vaccination

According to Public Health England, cases of whooping cough are expected to rise over the summer months. Local National Health Services (NHS) and public health teams increase their efforts to vaccinate pregnant women.

Whooping cough is caused by the highly contagious bacterium Bordetella pertussis. As the name says, the infection of the lungs and airways is accompanied with intense bouts of coughing followed by a distinct whooping sound. Other symptoms include a runny nose, raised temperature and vomiting after coughing. The infection can last for around three months, and may be passed from person to person through droplets in the air from coughing and sneezing. If it is diagnosed during the first three weeks of infection, a course of antibiotics may be prescribed. Most whooping cough cases occur in adults whose immunity faded after receiving vaccination as a child. Babies under the age of six months are most at risk of hospitalization from whooping cough, because they are most susceptible to complications.

Vaccination of pregnant women can give the babies protection until they are old enough to have their routine vaccinations. Nursing in Practice estimates that ~60% of eligible pregnant women take the vaccine.

Recently, experts at the UK-based online pharmacy ChemistDirect, urged pregnant women to get vaccinated against B. pertussis in order to protect the baby against whooping cough after birth. “Whooping cough tends to be cyclical, peaking every five years or so,” said Dr Omar El-Gohary, the superintendent pharmacist at ChemistDirect. “It is more endemic in summer/autumn and we are having one of those peaks right now. Those at higher risk include neonates especially as UK immunization programs start at two months old. It is therefore essential that all pregnant women over 28 weeks get vaccinated to pass on this immunity through the placenta.”

New nano-coating developed to preserve vaccines

Scientists at the University of Bath (UK) have been working on developing a nano-coating that could protect a vaccine from its environment both in transit and for storage. The new technique could potentially replace the complicated and costly cold-chain required for vaccines.

Even though most vaccines are stable below or around room-temperature, they degrade over time if not refrigerated. Delivery and storage of vaccines poses a big challenge for public health officials, especially in developing countries. Wastage of vaccines may leave vulnerable patients without protection and costs associated with transportation and storage are very high.

Using the latest advances in chemistry, researchers from the University of Bath want to show how nano-silica can be grown around individual vaccine molecules, enabling the vaccine to be taken anywhere in the world without refrigeration. The technique would produce a lightweight, easy-to-transport, solid material packed with vaccine. Once doctors were ready to administer the vaccine, the protective coating could be broken using either chemical or physical methods, such as acid or microwaves. Dr Asel Sarbaeva, a silica expert in the Department of Chemistry at Bath University, was recently short-listed for the prestigious L’Oreal Unesco Women in Science Fellowship for her work on this subject.

She said: “I am excited that my knowledge of silica can be used to help solve such a complex issue as cold chain—our dependence of constant vaccine refrigeration—which leads currently to a large waste of vaccines and threatens vaccination programmes worldwide. Once we can show that silica is the right material for vaccine preservation and storage, it will help save millions of lives and I am hopeful it will help us eradicate many vaccine-preventable diseases.”

Alternative approach to creating a universal flu vaccine

According to a new study published in The Journal of Experimental Medicine, it might be possible to stimulate the immune system against multiple strains of influenza virus by sequentially vaccinating individuals with distinct influenza strains isolated over the last century. The immune history was found to shape specificity of pandemic H1N1 influenza antibody responses.

Human antibody responses against the 2009 pandemic H1N1 (pH1N1) virus are predominantly directed against conserved epitopes in the stalk and receptor-binding domain of the hemagglutinin (HA) protein. This is in stark contrast to pH1N1 antibody responses generated in ferrets, which are focused on the variable Sa antigenic site of HA. In the current study, researchers from the Wistar Institute in Philadelphia showed that most humans born between 1983 and 1996 elicited pH1N1 antibody responses that are directed against an epitope near the HA receptor-binding domain. Importantly, most individuals born before 1983 or after 1996 did not elicit pH1N1 antibodies to this HA epitope. The HAs of most seasonal H1N1 (sH1N1) viruses that circulated between 1983 and 1996 possess a critical K133 amino acid in this HA epitope, whereas this amino acid is mutated or deleted in most sH1N1 viruses circulating before 1983 or after 1996. The researchers sequentially infected ferrets with a 1991 sH1N1 virus and then a pH1N1 virus. Sera isolated from these animals were directed against the HA epitope involving amino acid K133. These data suggest that the specificity of pH1N1 antibody responses can be shifted to epitopes near the HA receptor-binding domain after sequential infections with sH1N1 and pH1N1 viruses that share homology in this region.

Since influenza virus changes rapidly, new vaccines must be developed every year. A universal flu vaccine could negate the need for an annual influenza vaccination. Most current efforts to create universal vaccines
hinge on the idea of generating antibodies against a portion of the virus that is relatively unchanged year-to-year. The new results from Wistar researchers, could lead to an alternative approach to creating a universal flu vaccine.

“Our studies demonstrate that individuals that are infected sequentially with dramatically different influenza strains mount antibody responses against a conserved region of influenza virus,” said study senior author Scott Hensley from Wistar Institute. “Since we now know that pre-exposure events can influence vaccine responsiveness in a predictable way, we can begin to design vaccine regiments that preferentially elicit antibody responses against conserved regions of influenza virus.”

According to Dr. Hensley, one strategy would be to sequentially vaccinate children with antigenically distinct viral strains: “Babies are born with an immunological blank slate. We may be able to strategically vaccinate our children with antigenically diverse influenza strains to elicit antibodies against conserved viral epitopes.”

New modular vaccine design: MAPS technology

A team of researchers from Boston Children’s Hospital and Harvard Medical School recently presented a new method of vaccine design, called the Multiple Antigen Presentation System (MAPS). The new technology could unite the benefits of whole-cell and acellular or defined subunit vaccination.

Most current vaccines can be divided in three broad categories: live attenuated vaccines, whole-cell vaccines (WCVs), which rely on weakened or killed bacteria or viruses, and subunit vaccines, which include a limited number of defined antigens. Because of safety and reproducibility concerns, WCVs have been mostly replaced by subunit vaccines. However, subunit vaccine are generally less effective due to limited antigen diversity and reduced immunogenicity, especially in a lack of activation of antigen-specific T-cell immunity, which plays an important role in protection against mucosal and intracellular pathogens.

The MAPS method enables the linkage multiple protein and polysaccharide antigens from one or more pathogens in a modular fashion, using the interaction of two compounds, biotin and rhizavidin. Biotin is bound to the polysaccharide(s) of choice and rhizavidin to the protein(s). The two compounds bind together through an affinity interaction, thereby linking the polysaccharides with the proteins. The resulting complex, resembling a scaffold of polysaccharides studded with proteins, can stimulate both antibody and T-cell responses simultaneously, much like WCVs, resulting in stronger immunity to the source pathogens. The risk of side effects should be reduced, because the composition of MAPS vaccines is well defined and based on the use of isolated antigens.

Using antigens from various pathogens (Streptococcus pneumoniae, Salmonella typhi, and Mycobacterium tuberculosis), the researchers demonstrated the versatility of the MAPS system and its feasibility for the design of unique defined-structure subunit vaccines to confer comprehensive protection via multiple immune mechanisms. Moreover, they showed that MAPS could also serve as a tool for structure-activity analysis of cellular immunogens. Study results were presented in the journal Proceedings of the National Academy of Sciences of the United States of America.

Initial work has focused on bacterial pathogens, but Dr. Richard Malley, senior author of the current Proceedings of the National Academy of Sciences of the United States of America study, believes the technology could impact vaccine development for a broad range of pathogens, in particular those of importance in the developing world. “Technically, one could construct MAPS vaccines for viruses, parasites, even cancer antigens,” he said. “And the modularity is such that one could include antigens from multiple pathogens into the same vaccine, allowing the development of combinatorial vaccines much more efficiently.”

Reference

6. Li Y, et al. J Exp Med 2013; 210:1493-500; PMID:23857983; http://dx.doi.org/10.1084/jem.20130212

7. Zhang F, et al. Proc Natl Acad Sci U S A 2013; 110:13564-9; PMID:23898212; http://dx.doi.org/10.1073/pnas.1307228110