Cancer Vaccines

Christopher V. Chambers, MD

KEYWORDS

• Cancer • Vaccine • Prophylactic • Therapeutic

Vaccines have the potential to boost the immune system's ability both to prevent the infections that cause some cancers and to help the immune system identify altered or abnormal cells, including cancer cells, in the treatment of other cancers. Preventive, or prophylactic vaccines, work primarily by stimulating the production of antibodies by B cell lymphocytes. These antibodies bind to the targeted microbes and block their ability to cause infection that can lead to cancer. Prophylactic cancer vaccines, which include those directed at hepatitis B virus (HBV) and human papillomavirus (HPV), also work by boosting cellular immunity. In addition, cytotoxic T cells, or so-called killer T cells, are recruited to help kill already infected cells that have been identified by the immune system as altered, or prompt these cells to self-destruct (a process known as apoptosis). Cancer treatment vaccines, which are also referred to as therapeutic vaccines, work by activating B cells and killer T cells and helping them to recognize and act against cancer cells. In some cases, this involves isolating an antigen from cancer cells taken from the affected patient and creating a vaccine to present the antigen back to the patient, thereby stimulating the immune system to attack the cancer. Helper T cells and dendritic cells help activate killer T cells as part of the cellular immune response. There are many therapeutic cancer vaccines currently being evaluated in clinical trials, most of which are given in combination with other forms of cancer therapy. The first cancer treatment vaccine to be approved by the US Food and Drug Administration (FDA) (in 2010) is indicated for use in some men with metastatic prostate cancer.

CANCER PREVENTION VACCINES

Hepatitis B Vaccine

Liver cancer is the third leading cause of cancer-related deaths in the world and the ninth leading cause of cancer deaths in the United States.[1,2] Nearly 80% of all cases are associated with underlying chronic hepatitis B or hepatitis C infection.[3] In the United States, hepatocellular carcinoma (HCC) occurs predominantly in adults, many of whom acquired hepatitis B or C through intravenous drug use. In other parts of the world, such as southeast Asia, where hepatitis B infection is endemic, HCC occurs in persons of all ages, including children. Although epidemiologic evidence

Department of Family and Community Medicine, Jefferson Medical College, Thomas Jefferson University, 1015 Walnut Street, Suite 401, Philadelphia, PA 19107, USA
E-mail address: Christopher.Chambers@jefferson.edu

Prim Care Clin Office Pract 38 (2011) 703–715
doi:10.1016/j.pop.2011.07.008 **primarycare.theclinics.com**
0095-4543/11/$ – see front matter

has established that chronic HBV infections are associated with the development of HCC, the mechanism of oncogenic transformation remains elusive. Multiple studies have implicated a protein known as the HBV X protein (HBX) as playing an important role.[4,5] HBX regulates several cellular signal transduction pathways including those that modulate cell proliferation. HBX also indirectly or directly affects the levels and activities of several other cell cycle regulatory proteins that, working in combination, can induce normally quiescent cells to replicate. This process may help explain why HCC can develop in patients with apparently inactive infection after many years. Treatments for chronic HBV infection and for HCC have not been successful and efforts have focused instead on prevention.

The original hepatitis B vaccine was approved in 1981, making it the first cancer prevention vaccine to be successfully developed and marketed. In 1984, Taiwan launched the world's first universal HBV vaccination program for infants.[6] The effectiveness of the hepatitis B vaccine in preventing HCC in Taiwan has been dramatic and was measurable in children within 2 decades. With the introduction of the universal vaccination program, all newborn infants were given a series of 3 or 4 doses of recombinant hepatitis B vaccine. In addition, infants of highly infectious (positive to the hepatitis B e antigen [HBeAg]) mothers received hepatitis B immunoglobulin within 24 hours of birth. Nearly all eligible infants were vaccinated as part of the program. The overall immunization rate was reported at 97%. After 20 years, the seroprevalence of the hepatitis B surface antigen (HB_SAg) in children declined from 9.8% (prevaccination period) to 0.6%.[7] This decrease in infection was associated with a significant reduction in childhood HCC (**Table 1**). In a 13 year period (1981–1994), the incidence of HCC in children between 6 and 9 years old declined from 0.52/100,000 for children born between 1974 and 1984 to 0.13/100,000 for those born between 1984 and 1986 ($P<.001$). The HCC cases that were not prevented by the vaccine program were subsequently investigated in an evaluation of the program. In more than 90% of the HCC cases, both the affected child and the mother, were HB_SAg-positive in spite of the universal vaccination program. The vaccine failure has been attributed to poor compliance with the 3-shot series, genetic hyporesponsiveness (to the vaccine), and vaccine escape mutants (viruses with enough antigenic changes to avoid immune recognition).[8]

The hepatitis B vaccine has been clearly shown to be an effective, preventive vaccine against HCC. Consequently, all infants are immunized routinely. The duration of the protective effect in healthy individuals is not known and the need for boosters in the at-risk population has not been defined. Adults at high risk because of possible exposure to blood or because of chronic hepatitis C should also be immunized. Booster vaccinations should be considered in some particularly high-risk groups.

HPV INFECTION

Epidemiology

HPV infections are now recognized as the cause of multiple human cancers, most prominently cervical cancer. Worldwide, cervical cancer is the second most common

Table 1
Effect of universal hepatitis B vaccination of infants in Taiwan (1984)

	% HB_SAg-Positive (All Children)	HCC Incidence per 100,000 (6–9 Years Old)
Before 1984	9.8	0.52
After 1984	0.6	0.13

Data from Ni YH, Chen DS. Hepatitis B vaccination in children: the Taiwan experience. Pathol Biol 2010;4:296.