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Vaccines:

An Emerging Multi-Modal Tool in the Fight Against Cancer

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Abstract

Vaccines play an import role in cancer prevention as well as a growing role in cancer therapeutics. This article explores current knowledge regarding the role of vaccines (HPV and HBV vaccines) in protecting against preventable risk factors for select cancers as well as anti-cancer vaccines currently being used in practice. Current data suggests that routine childhood vaccination against HPV and HBV is an effective strategy for not only protecting against life-altering infectious diseases but also protecting against adult-onset cancers. Furthermore, while current vaccination practices and anti-cancer therapeutics have come a long way in recent decades, examination of CDC data also identifies areas for growth and improvement.

Introduction

Vaccines are commonly known for their significance in preventing a wide range of infectious diseases. However, they also play an essential role in cancer prevention and have an emerging role in treating select cancers. An estimated 12% of cancers worldwide are linked to viruses (Epstein-Barr Virus, Hepatitis B, Hepatitis C, Human papilloma virus),[1] thus highlighting the importance of exploring the intersection of infectious diseases and oncologic processes. Routine childhood immunizations such as the Hepatitis B (HBV) and Human papilloma (HPV) vaccines protect against adult-onset malignancies such as hepatocellular carcinoma and HPV-associated cancers (e.g. cervical cancer, oropharyngeal cancer, oral cancer, and other genital cancers) respectively. The Bacillus Calmette–Guérin (BCG) vaccine, a vaccine used outside the US to prevent tuberculosis, is used an approved therapy for bladder cancer in the US.[2] Moreover, there are many cancer vaccines currently in development to treat a variety of solid organ and hematologic malignancies.[1] In this article, we will explore the impact and importance of vaccines in the fight against cancer.

Hepatitis B and Hepatocellular Carcinoma

HBV is a preventable risk factor for hepatocellular carcinoma (HCC), which is associated with high morbidity and mortality worldwide. The five-year rate of progression from chronic HBV to cirrhosis is estimated to be anywhere between 12-20%.[3] Of those affected by cirrhosis, the cumulative five-year progression rate to hepatocellular carcinoma is estimated to be about 10% in the US.[3] Moreover, there is global variability in the prevalence of HBV-associated HCC. In areas of the world where HBV is hyperendemic such as Asia, HBV is responsible for up to 50% of HCC. There is a lower prevalence of HBV-associated HCC in the US, which is suspected to be due to relatively high vaccination rates against HBV.[4] It is important to note that infants infected with HBV are at significantly higher risk for developing chronic HBV compared to adults. While only about 5% of adults infected with acute HBV do not clear the infection and progress to chronic HBV, about 90% of infected infants progress to chronic HBV infection.[5]

Thus, early vaccination against HBV, particularly the birth dose of HBV, as well as screening for perinatal exposure is critically important. Nationwide, an estimated 25,000 infants are born to HBV carriers[6] and of those perinatally exposed infants, about 90% are estimated to acquire an HBV infection without preventive measures.[5] In the US and many countries in the world, the HBV vaccine is routinely given within the first 12-24 hours of life as well as 2-3 additional times within the first six months of life. This method has proven to be efficacious as the proportion of children under the age of five with chronic HBV was estimated to be less than 1% in 2019, a significant decrease from around 5% in the 1980s prior to the implementation of the HBV vaccine.[7] While there has been a lot of progress in HBV prevention, there is still room for improvement. In 2020, about 80.6% of infants born in the US that year received the birth dose of Hep B within the first 48 hours of life.[5,8] In that same year, the percentage of toddlers (aged 35 months) and adolescents (13-17 years old) who had received three Hep B doses were approximately 92.9% and 92.6% respectively.[5] Given the high risk of vertical transmission and high risk of progression to chronic HBV in infants, this discrepancy between vaccination of newborns vs. older children and adolescents highlights an area for improvement.

Furthermore, acute HBV infection is oftentimes asymptomatic, putting infected adults particularly at risk for transmission. Approximately 30% of adults aged 19 and older were self-reported to have been fully vaccinated against Hep B.[5] This may be due to a variety of factors including the fact that the first HBV vaccine was approved by the FDA in 1982. Therefore, as of 2023, the CDC updated HBV screening guidelines to include one-time triple panel screen (HBsAg, anti-HBs, total anti-HBc) for HBV for adults 18 and older in the general population in addition to the previous screening guideline for pregnant women and those at increased risk for HBV infection (e.g. patients with HCV or HIV, high risk sexual activity, IV drug use, and others).[5]

HPV and HPV-Associated Malignancies

HPV is associated with multiple genital malignancies (cervical, vulvar, vaginal, anal, penile cancer) as well as squamous cell carcinomas of the head and neck (oral, oropharyngeal, laryngeal cancer). Of particular importance, HPV is a major preventable risk factor for cervical cancer. Recent studies show that over 90% of cervical cancers are linked to HPV.[9] Thus, immunization against HPV is imperative in preventing cervical cancer. Globally, cervical cancer is the fourth most common malignancy in women and is estimated to cause over 311,000 cancer deaths annually.[9] Multiple studies have shown the efficacy of the HPV vaccine in reducing rates of cervical cancer, with rates of risk reduction as high as 87% pre and post vaccine era.[10] HPV 16 and 18, which are particularly oncogenic, account for about 70% of cervical cancer cases. HPV 31, 33, 45, 52, and 58 are also considered high risk for causing cervical cancer and altogether account for 19% of cases. The 9-valent HPV vaccine available in the U.S. protects against subtypes 6, 11, 16, 18, 31, 33, 45, 52, and 58, providing protection against the most high-risk oncogenic subtypes of HPV. Per the most recent CDC Morbidity and Mortality Weekly Report (MMWR), only about 76% of adolescents aged 13-17 nationwide had received one or more HPV vaccines, and about 62.6% were fully up to date with HPV vaccines.[11] The vaccination rates of HPV are notably lower than those of other recommended adolescent vaccines (89.9% and 88.6% for Tdap and MenACWY respectively) (Table 1).[12] Additionally, HPV vaccination rates are overall higher in Delaware for both males and females compared to the national averages (Table 2).[12] Of note, the percentage of teens up to date on their HPV vaccine is more than 10% lower than the percentage vaccinated with one HPV dose across the board for both males and females,

in Delaware and nationwide. This disparity in vaccination highlights a clear area for improvement with regard to HPV and HPV-associated cancer prevention.

Table 1. Comparison of Vaccination Rates in Adolescents (aged 13-17) in the US[11]

Vaccine	HPV	Tdap	MenACWY
% Vaccinated with at least 1 dose	76%	89.9%	88.6%

Table 2. Comparison of Vaccination Rates of HPV in Adolescents (aged 13-17) in Males and Females in Delaware and in the US, Based on 2022 CDC Data[12]

	% Vaccinated with at Least 1 Dose	% Up to Date on Vaccine
Males in Delaware	85.8%	68.8%
Females in Delaware	82.6%	67.5%
Males Nationwide	74.4%	60.6%
Females Nationwide	77.8%	64.6%

Therapeutic Vaccines

Vaccines also have a role in the treatment of cancer. The most long-standing example is the BCG vaccine, a live attenuated strain of *Mycobacterium bovis* that is used in many countries outside the US to prevent tuberculosis. In the US, it has become a mainstay of treatment for intermediate to high-risk non-muscle invasive bladder cancer (NMIBC). Intravesical treatment with BCG has been proven to be efficacious in reducing the risk of post-resection recurrence of NMIBC when used as a post-surgical adjuvant treatment. Early studies showed a five-year recurrence-free survival rate as high as 80% in those treated with adjuvant BCG after bladder tumor resection compared to those treated with resection alone.[2] Subsequent landmark studies found that patients with NMIBC treated with intravesical adjuvant BCG even had higher recurrence-free survival rates than those treated with traditional intravesical chemotherapeutic agents such as doxorubicin and mitomycin. Thus, over the past 40 years, post-resection adjuvant intravesical BCG treatment has become the standard of care for NMIBC.[2] It is also worth noting that other therapeutic cancer vaccines, although they are not antimicrobial vaccines, work by targeting a patient's own immune response against tumor cells, and are considered a subtype of immunotherapy. For example, Provenge (Sipulecel-T) is a cell-based cancer vaccine FDA-approved for the treatment of metastatic castration-resistant prostate cancer. It works by targeting a patient’s own dendritic cells against prostate cancer tumor cells.[13] There are many types of cancer vaccines currently in development against a wide range of cancers including pancreatic cancer, non-small cell lung cancer, multiple myeloma, and many more.[1]

Conclusion and Perspectives

Vaccination is both an effective prevention strategy against cancer as well as an emerging therapy. This article summarizes well-established and widely implemented prevention strategies such as the HBV and HPV vaccines. Improving current vaccination rates against HPV and HBV present feasible avenues for improving cancer prevention. Moreover, the BCG vaccine and Provenge demonstrate the viability and promising therapeutic potential of anticancer vaccines. While Provenge is a cell-based vaccine, there are currently numerous clinical trials exploring the use of different vectors including virus-based, peptide-based, and nucleic acid-based anti-cancer vaccines (e.g. mRNA, DNA).[1]

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