Bivalent vaccine is effective against HPV for 4.5 years

Clinical question Does a vaccine confer long-term protection against human papillomavirus (HPV) strains associated with cervical cancer?

Bottom line A bivalent vaccine against HPV types 16 and 18 is well tolerated and effective in reducing HPV infection and HPV-associated cytologic abnormalities for 4.5 years. (Level of evidence = 1b)

Harper DM, Franco EL, Wheeler CM, et al, for the HPV Vaccine Study group. Sustained efficacy up to 4.5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: follow-up from a randomised control trial. *Lancet*. 2006; 367:1247-1255.

Synopsis We previously reviewed the initial report from this study (*Lancet*. 2004;364:1757-1765) that demonstrated after 27 months that a bivalent vaccine active against HPV serotypes 16 and 18 was more effective than placebo in reducing HPV infection and HPV-associated cytologic abnormalities. In this study, the investigators provide additional follow-up on 776 of 1,113 women from the original study who received all three doses of vaccine or placebo and for whom treatment allocation remained double blinded. In the original study, women were eligible if they were 15 to 25 years old, had had no more than six sexual partners, and had no history of condyloma or cervical cancer. The vaccine or placebo was administered at 0, 1, and 6 months. In the intention-to-treat analysis for the subsequent follow-up period, the absolute reduction in new HPV infections was 7.4% (number needed to treat [NNT] = 14; 95% CI, 10-23). If the results for events occurring during the initial study period are combined with the results from this follow-up period, the absolute reduction is 13.7% (NNT = 8; 6-10). Furthermore, no vaccinated woman developed HPV 16/18-associated dysplasia (and only 2 developed HPV 16/18-associated disease) compared with 1.7% of those receiving placebo (NNT = 59; 30-182). Interestingly, this vaccine also appeared to give some cross-protection against HPV 45 and HPV 31. Additional data and analyses are needed to understand the mechanisms of cross-protection and its importance to lesion development. Finally, the vaccine was well tolerated. A total of 14% of those vaccinated reported at least one adverse effect, compared with 22% of those receiving placebo; 3% reported at least one new onset of chronic disease, compared with 5% taking placebo; and 4% reported at least one serious adverse event, compared with 5% taking placebo.

Probiotics are helpful for antibiotic-associated diarrhea

Clinical question Can probiotics prevent antibiotic-associated diarrhea and assist in the treatment of *Clostridium difficile* disease?

Bottom line The probiotics *Saccharomyces boulardii* and *Lactobacillus rhamnosus* GG both prevent antibiotic-associated diarrhea (AAD), as does a combination of two or more probiotics. *S boulardii,* given in addition to vancomycin or metronidazole, is also an effective treatment for *C difficile* disease (CDD). (Level of evidence = 1a-)

McFarland LV. Meta-analysis of probiotics for the prevention of antibiotic associated diarrhea and the treatment of *Clostridium difficile* disease. *Am J Gastroenterol*. 2006;101:812-822.

Synopsis A variety of probiotics have been proposed to help reestablish the gut flora, prevent AAD, and treat CDD. This meta-analysis identified any blinded, randomized, controlled trials (RCTs) on MEDLINE and Google Scholar and evaluated their quality. There were 25 RCTs of AAD prevention including 2,810 patients and six RCTs of CDD treatment including 354 patients. Studies were generally of good quality. There was considerable heterogeneity regarding population and results for studies of prevention of AAD. Although there was no difference in outcomes for studies in adults or children, or by duration of therapy, a greater benefit was seen for studies using a higher dose. *S boulardii* and *L rhamnosus* GG, both studied in six RCTs, were most effective (combined relative risk = 0.37 and 0.31, respectively) as was a combination of two probiotics. In most studies of CDD treatment, patients were also given vancomycin or metronidazole, and the outcome was the likelihood of recurrence of disease. Results of the six studies were homogeneous, and a combined estimate of effect showed a relative risk of recurrent CDD of 0.59 (95% CI, 0.41-0.81). *S boulardii* seemed to be the most effective probiotic. Adverse effects in both sets of studies were minimal. These studies took place largely in immunocompetent patients, and results should not be generalized to apply to immunocompromised patients.

Hot-water immersion is best for Portuguese man-of-war stings

Clinical question Is hot-water (45ºC, 113ºF) immersion more effective than ice-pack application for relief of pain caused by bluebottle jellyfish stings?

Bottom line Immediate hot-water immersion for up to 20 minutes is significantly more effective than ice-pack application for pain caused by bluebottle jellyfish (Portuguese man-of-war) stings. (Level of evidence = 1b-)

Loten C, Stokes B, Worsley D, et al. A randomized controlled trial of hot water (45° C) immersion versus ice packs for pain relief in bluebottle stings. *Med J Aust*. 2006;184:329-333.

Synopsis Bluebottle jellyfish (Portuguese man-of-war) stings can cause significant pain that usually resolves within 1 hour. Most first-aid organizations recommend the application of ice packs. To evaluate the potential effectiveness of hot-water immersion (since many marine venoms are heat labile in vitro), the investigators randomized (uncertain allocation concealment) 96 patients with an apparent bluebottle sting at two beaches in eastern Australia to either hot-water immersion or ice-pack application. Accurate water temperature at 45ºC (113ºF) was ensured by using thermostatic mixing valves to prevent superficial burns. Patients self-reported pain levels at baseline and at 10 and 20 minutes after treatment using a visual analog scale (VAS) of 0 to 100. The primary outcome was a clinically important reduction in pain, defined as a change in millimeters on the VAS scale dependent on the baseline starting point (16 mm for an initial VAS of 0-33 mm; 33 mm for an initial VAS of 34-66 mm; and 48 mm for an initial VAS of 67-100 mm). One investigator microscopically evaluated adhesive tape placed over all sting sites to confirm the presence of nematocysts. Follow-up occurred for 92% of the patients at 20 minutes. Analysis was by intention to treat. At 10 minutes, 53% of the hot-water treatment group reported a clinically significant reduction in pain, compared with 32% treated with an ice pack (number needed to treat [NNT] = 5; 95% CI, 3-72). At 20 minutes, 87% of the hot-water treatment group reported a clinically significant reduction in pain, compared with 33% treated with an ice pack (NNT = 2; 1-3). Radiating pain also occurred significantly less with hot water, and no patients suffered burns from hot-water immersion. Nematocysts were confirmed in 42 (44%) of the subjects. Hot-water immersion remained significantly more effective than ice packs in an analysis of only those patients with nematocyst-confirmed stings. Itch, redness, and rash at 24 hours occurred similarly in both groups.

Levels of evidence are explained at http://www.infopoems.com/levels.html.

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