

## Compulsory HPV Vaccination

**TO THE EDITOR:** In his Perspective article on the ethics and politics of compulsory vaccination against human papillomavirus (HPV) (Dec. 7 issue),<sup>1</sup> Colgrove highlights the perception that HPV vaccination is a women's health issue, yet he also alludes to the question of how much herd immunity may be necessary to protect unvaccinated women from cervical cancer. Exploration of the question of herd immunity exposes HPV vaccination as a men's health issue as well — that is, men are responsible for half the cases of transmission of the virus, and vaccinating men, if found to be effective in reducing the transmission of HPV to women, could be an important mechanism for reducing the burden of cervical cancer. At least one recent study involving boys has reported noninferior immunogenic responses to all four types of HPV covered by the quadrivalent vaccine.<sup>2</sup> We have insufficient data to evaluate how great an effect vaccinating boys could have on reducing transmission to women. Therefore, the possibility of vaccinating persons of both sexes should be further evaluated if we are to consider all policy options for preventing cervical cancer.

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**TO THE EDITOR:** The political implications of compulsory HPV vaccination deserve further attention. Unfortunately, Colgrove only briefly mentions Michigan's proposed legislation regarding HPV vaccination, and he erroneously describes it as compulsory vaccination. What Michigan's proposed legislation actually requires is that parents receive information on the connection between HPV and cervical cancer before making an informed decision about HPV vaccination for their adolescent daughters.<sup>1</sup> This broad allowance for informed refusal — for any reason — is clearly outside the realm of traditional programs of compulsory vaccination, which permit only religious or medical exemptions. By allowing informed re-

fusal, Michigan's ingenious proposed legislation not only respects individual liberties but also ensures that all adolescent girls will be offered the vaccine and eliminates the opportunity for passive omission by parents and physicians. Other states considering HPV-vaccination legislation should take a serious look at Michigan's proposed legislation and follow its lead in balancing individual liberties with the legitimate health concerns raised by HPV and cervical cancer.

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1. Michigan Senate bill 1417 (as passed on Sept. 20, 2006).

**THE AUTHOR REPLIES:** Basu makes an important point about the indirect effect that vaccinating boys against HPV might have on the incidence of cervical cancer among women. A policy of vaccinating one segment of the population for the primary purpose of reducing the incidence of a disease in another segment was also undertaken in the case of the rubella vaccine, which is routinely given to all children for the primary purpose of reducing the incidence of congenital defects in infants born to women who contract rubella during pregnancy.<sup>1</sup>

Segraves is incorrect in stating that a vaccination law allowing informed refusal for any reason “is clearly outside the realm of traditional programs of compulsory vaccination, which permit only religious or medical exemptions.” Almost half the states that allow exemptions for medical or religious reasons also permit exemptions for personal or philosophical concerns. It is true that a law such as Michigan's that contains an opt-out provision does not represent compulsion in a strict sense,<sup>2</sup> but as used in common parlance, the term “compulsory” applies to school-based vaccination policies in the United States. Some states place administrative burdens on parents who seek exemptions — such as requirements to obtain a form from a local health department, to write a letter explaining their decision, or to renew the exemption annually — that may in practice make it difficult to claim an exemption.<sup>3,4</sup>

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## Retraction: Guo H. Complication of Central Venous Catheterization. *N Engl J Med* 2007;356:e2

**TO THE EDITOR:** I retract the Image in Clinical Medicine presenting a complication of central venous catheterization that was published in the January 11, 2007, issue of the *Journal*,<sup>1</sup> because the figures, which I had previously submitted elsewhere, have already been published.<sup>2,3</sup>

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1. Guo H. Complication of central venous catheterization. *N Engl J Med* 2007;356:e2 (Web only). (Available at <http://content.nejm.org/cgi/content/full/356/2/e2>.)
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## Prolonged Bisphosphonate Release after Treatment in Children

**TO THE EDITOR:** Bisphosphonates are widely used in the management of osteoporosis. They are cleared rapidly from the circulation, with about half the administered dose taken up by the skeleton and the rest excreted unmetabolized by the kidneys.<sup>1</sup> At the bone surface, bisphosphonates suppress bone resorption and are embedded in bone. The embedded bisphosphonate is released slowly from bone, presumably after the resumption of bone remodeling at previously exposed sites.

A terminal half-life of 10 years has been estimated for alendronate in the longest pharmacokinetic study in humans, up to 1.5 years, after intravenous administration. There is no direct evidence of release of bisphosphonates in patients who receive long-term, continuous oral treatment, the most common therapy for osteoporosis. Such information can help explain changes in bone remodeling and in bone mineral density after the cessation of long-term treatment and can be obtained by measuring the urinary excretion of bisphosphonates, the only route of their elimination from the body.

We measured drug excretion after the cessa-

tion of long-term treatment with daily oral pamidronate in seven young patients with severe osteoporosis — four with juvenile osteoporosis, two with osteogenesis imperfecta, and one with juvenile arthritis. All but one of the patients has been described previously<sup>2</sup>; all had normal renal function. At the start of treatment, the patients were between the ages of 10 and 14 years, and they received pamidronate for a mean period of 6.7 years (range, 4 to 10). Excretion of pamidronate was measured in 24-hour urine samples with the use of fluorometry and high-performance liquid chromatography at a mean interval of 7.7 years (range, 3 to 12) after treatment had been discontinued; the total mean observation period was 12.9 years (range, 7 to 19).

Pamidronate was detectable in urine samples from the patients up to 8 years after the cessation of treatment (Fig. 1A). There was a trend toward reduced excretion of the drug with time, but there was no relation between the cumulative dose of the bisphosphonate and its excretion in urine (Fig. 1B).

These results provide direct evidence of long-term release of a bisphosphonate and show that