

Acute hepatitis A virus infection: a review of prognostic factors from 25 years experience in a tertiary referral center. *Hepatogastroenterology* 2002;49:524-8.

**THE AUTHOR REPLIES:** In response to Betz: although the relative risk indicated an approximately 30% higher risk among recipients of vaccine than among recipients of immune globulin, absolute risks were low, and absolute risk differences were never greater than 1.5%. Still, in our report, my colleagues and I draw attention to the potential relevance of these differences for persons who are likely to have severe illness if infected with the hepatitis A virus. Indeed, the Advisory Committee on Immunization Practices considered these small differences when updating recommendations for postexposure prophylaxis.<sup>1</sup>

Several of Betz's characterizations of our findings merit clarification. It is arguable whether the proportions of vaccine recipients and immune-globulin recipients with detectable hepatitis A virus RNA (62% and 56%, respectively;  $P=0.761$ ) are different; they might equally well be considered equivalent. As we noted, the study was not designed to measure disease severity. Furthermore, alanine aminotransferase levels should be interpreted with caution, since measurements were performed once at nonstandardized time points during the course of the illness; in addition, differences were limited to levels among children. Finally, although in the modified intention-to-treat population, the relative risk with vaccine as compared with immune globulin was lower in the first week after exposure than in the second week, in the per-protocol population, it was higher in the first week after exposure than in the second week (1.73 vs. 1.30).

Betz's statement that "immune globulin has a time-dependent advantage over the delayed development of vaccine-generated antibodies" appears to be based on the assumption that hepatitis A vaccine used after exposure operates solely through antibody-dependent mechanisms. However, antibody-independent T-cell effects may be important, and vaccination after exposure might modulate an already initiated immune response in participants with incubating hepatitis A virus — something immune globulin is unlikely to do.

Unlike Lee, we believe that our study results are applicable to persons in developed countries. Our analyses of relative efficacy were conducted among only those persons found to have been susceptible at the time of receipt of vaccine or immune globulin, precisely so that conclusions would be applicable to susceptible persons in any population. Moreover, the generalizability of the results is supported by studies of the transmission dynamics of hepatitis A virus in the population, conducted before implementation of the trial.<sup>2,3</sup>

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## Children and the Quality of Ambulatory Care

**TO THE EDITOR:** Mangione-Smith et al. (Oct. 11 issue)<sup>1</sup> report that children receive only 46.5% of recommended health care. Is our goal 100% adherence to these recommendations? What are barriers to improvement?

Hayward commented, regarding performance-measure adherence for adults, "It sounds terrible . . . that 50% of recommended care is not received, but . . . mandating adherence to these recommendations is not necessarily in the best interest of patients or society. . . . At the heart

of this problem is our wish to keep efforts at quality improvement and cost containment separate."<sup>2</sup> Benefits from guidelines are not necessarily additive,<sup>3,4</sup> since there are usually costs and sometimes unintended consequences.<sup>5</sup>

Although many believe that children, with their developmental needs and relative dependence, deserve unlimited health care resources, such resources do not appear to be available currently. Choices are necessary. For example, should we give priority to hospitalizing young febrile

infants,<sup>1</sup> or instead provide immunizations, health insurance, pharmaceuticals, or developmental or mental health services or both? Ignoring cost-effectiveness often results in illogical rationing of care.

I hope that this important study will catalyze discussion regarding our society's priorities for children, our most precious national resource.

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## Hair Loss in Women

**TO THE EDITOR:** In the Clinical Practice article on hair loss in women by Shapiro (Oct. 18 issue),<sup>1</sup> the assertion that "the yield of testing [for hormonal causes of female-pattern hair loss] is expected to be low in the absence of other features suggesting androgen excess" is not supported by the cited series of patients with female-pattern hair loss.<sup>2</sup> Although the "majority" of patients in this series had normal serum androgen levels, 42 of 109 subjects had hyperandrogenism, as defined by an increase in testosterone, non-sex hormone-binding globulin-bound testosterone, dehydroepiandrosterone sulfate (DHEAS), androstenedione, or dihydrotestosterone.<sup>2</sup> In 2 of 44 patients, cosyntropin stimulation testing revealed 21-hydroxylase deficiency.<sup>2</sup> Although the generalizability of the findings in this series is limited, the polycystic ovary syndrome has become even more prevalent since their publication.<sup>3</sup> Likewise, nonclassic congenital adrenal hyperplasia is an occasional cause of hyperandrogenism in premenopausal women. A rapid onset of hyperandrogenism marked by hirsutism, acne, female-pattern hair loss, clitorimegaly, voice deepening, or menstrual irregularity warrants evaluation for ovarian and adrenal tumors, with measurement of total testosterone and DHEAS. Finally, hyperthecosis ovarii should be considered in postmenopausal women with slowly developing and often severe hyperandrogenism. These diseases are not just the domain of "interested endocrinologist[s]"<sup>4</sup> but the responsibility of all treating physicians.

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**THE AUTHOR REPLIES:** The general consensus in the dermatologic community is to order measurements of androgen levels for patients with female-pattern hair loss only if indicated.<sup>1</sup> For the first 5 years of my practice, I routinely ordered measurements of serum androgen levels in all my patients with female-pattern hair loss. The yield of a positive result was extremely low for women without other clinical signs of androgen excess. Schlegel cites the study by Futterweit et al. However, this study population was not representative of the general population, since many of the patients had been referred to endocrinologists.

Dermatologists and family physicians see the vast majority of women with female-pattern hair loss. It has been estimated that 38% of women in the general population have female-pattern hair loss.<sup>2</sup> Most of these millions of women do not have clinical signs of androgen excess. Evidence to support routine testing for hyperandrogenism in such women is lacking. I agree with Schlegel, however, that the possibility of androgen excess should routinely be considered in patients with female-pattern hair loss.

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