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The above letter was referred to the author of the article in question, who offers the following reply.

To the Editor: Dr. Harper makes some excellent points in her letter. The field of cervical cancer diagnosis and treatment is rapidly changing with new modalities being developed and introduced very quickly. Family physicians who perform colposcopy need to figure out a way to stay current with the overwhelming amount of recent literature in this field.

While the Virapap and Viratype test might now be considered outdated technology, it was the only test commercially available when the data were collected and hence constituted the most evolved technology at that time. Dr. Harper cites a number of references which she states document the difficulties with the Virapap and Viratype.[1-6] While human papillomavirus (HPV) testing is a part of the study methods of each of these reports, not all show "difficulties" with the test kit. In fact, Lorincz et al reports a sensitivity of 92 percent and a specificity of 89 percent (compared with cervical cytology).[1] The Lorincz et al paper and the article by Moscicki et al also compared HPV testing with cytology.[1,4] Cervical cytology cannot be considered a reference standard for diagnosis of HPV with its high false-negative rate. The Weintraub et al[5] study compared the Virapap/Viratype kit to polymerase chain reaction. Polymerase chain reaction might be a very sensitive method of HPV detection, but it is not the reference standard for clinicians.

A key point when evaluating a new diagnostic test is that one must compare it with the reference standard that is currently in use. Reported sensitivities and specificities for the Virapap/Viratype by Digene Diagnostics were 94.5 and 95.5 percent, respectively.[7] These results were obtained when comparing the dot blot DNA hybridization of the Virapap/Viratype kit with the laboratory reference standard of Southern blot DNA hybridization. In clinical practice, the reference standard for HPV diagnosis is a colposcopy and directed cervical biopsies with histologic evaluation. Only the Reid et al study[2] used this method as their reference standard.

Dr. Harper cites four articles that show the Hybrid Capture method has "a marked improvement compared with the first-generation test." If by "marked improvement" she means an improved sensitivity, she is absolutely correct. The study by Sun et al[8] showed a calculated sensitivity of 79 percent compared with colposcopy and cervical histology. The article by Cox et al[9] demonstrates a sensitivity of 86 percent compared with colposcopy and cervical histology. Both of these studies show a decrease in specificity (58 percent and 71 percent, respectively), but for cervical cancer screening, a test with a higher sensitivity is preferred.

New diagnostic tests are being introduced regularly. When reading articles that evaluate their performance, be sure that the reference standard is easily recognized and that it is clinically applicable. I agree with Dr. Harper that the most technologically evolved test should be used when conducting research and that the role of HPV testing in cervical cancer screening remains to be elucidated. All family physicians who care for women should be aware of the evolving nature of cervical cancer screening and the need to stay clinically current.

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Management of Hepatitis C

To the Editor: I found the article by Salazar and associates[1] to be most helpful in further documenting the growing threat of hepatitis C virus (HCV) as it relates to chronicity. Current estimates are that 3.5 million Americans have chronic HCV.[2] A few critical points are worth mentioning or clarifying, however, as family physicians begin to screen more of their patients with elevated aminotransferases for HCV.

Much is still not known about HCV, and recent data have described at least five different serotypes of the virus, which has major implications for disease progression, treatment, and the development of an effective vaccine.[3] In regard to treatment, there is a growing consensus now recommending 12 months as opposed to 6 months of interferon alfa therapy.[4] This self-administered drug must be given three times weekly and is not without considerable side effects, including extreme fatigue, myalgias, and depression.[5] As a result, compliance is a major issue with interferon. Additionally, the cost of the drug, approximately $5000 for a 1-year course of therapy, might not be covered by third party payers. And finally, previous clinical trials found that only about 50 percent of treated patients will initially respond to interferon therapy, and one half of this group will ultimately relapse.

I believe the bottom line with HCV is that before screening patients, both physician and patient need to be well-informed of the consequences of the results. Liver biopsy, expensive long-term injectable therapy, and frequent follow-up blood testing, as well as the ultimate potential for liver transplantation, are just some of the issues that must be discussed with the patient. I hope future studies of viral serotypes, HCV RNA levels, and the use of other antiviral drugs will allow physicians to better predict a therapeutic course of action in those whom we are screening.

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The above letter was referred to the authors of the article in question, who offer the following reply.

To the Editor: We thank Dr. Kirchner for his interest and comments regarding screening patients at risk for hepatitis C and subsequent treatment of those with the disease. Dr. Kirchner was correct in pointing out the existence of several serotypes of the hepatitis C virus. In fact, there are currently six major serotypes with a total of 11 subtypes of hepatitis C.[1] Genotyping can be useful in assessing response to interferon and can assist in the selection of patients who will respond to interferon treatment.[2] HCV RNA levels have also been used in assessing response rate to treatment[3] in addition to interferon dose, liver histology, and duration of treatment. Prolonged treatments of HCV for 12 to 18 months have been shown to result in a better response in patients than the conventional 6 months of treatment,[4] even in the absence of favorable biochemical response. At this point, the treatment is less than optimal, and further studies will be necessary to evaluate current and new therapies.

As family physicians, we are faced with the challenge of keeping up with the ever-growing knowledge of viral hepatitis and its treatment and the wide array of hepatotropic viruses recently discovered[5] and those that yet have to be identified. We continue our efforts in the identification of hepatitis C and hope that others in the field of medicine will continue their search for better therapy.

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