

program has increased steadily to 94 percent. Contrary to Udawadia's assertion, areas that fail to enroll a high proportion of patients in the program tend to have lower cure rates — a reflection of weaker implementation of the program. For example, the area with the lowest proportion of patients with diagnosed tuberculosis who were treated in the program in the most recent quarter was also the area with the lowest cure rate.<sup>1</sup> Direct observation is essential in the intensive phase of treatment, when the burden of organisms and the risks of treatment failure and development of drug resistance are highest; in the continuation phase, the program uses direct observation for at least the first of three doses per week.

The proportion of patients at a referral hospital who have multidrug-resistant tuberculosis has no relevance to the actual proportion of people in the community who have multidrug-resistant disease.<sup>2</sup> All valid studies in India have found rates of multidrug resistance of 1 to 3 percent among previously untreated patients.<sup>3-6</sup> Multidrug-resistant tuberculosis is a symptom of poor performance of programs; the highest priority is to prevent multidrug-resistant tuberculosis by effective treatment. As we state in our article, more than 1 million patients each year with newly diagnosed tuberculosis do not yet have access to basic treatment, and the top priority must be to ensure that they have such access. Both HIV-positive and HIV-negative patients are treated in the program; models to improve coordination are being evaluated.

With regard to the issues raised by Schaller and Starke, the new program includes treatment of children with active disease as well as investigation of

contacts and preventive treatment of children who are contacts of those with infectious cases. These efforts have met with varying degrees of success in different parts of the country.

There are several errors in our article. Clinical features are provided in Table 2, not Table 1. On page 1422, the top line of the right column should read "More than 200,000" rather than "Nearly 200,000." The sentence beginning on line 12 of that column should read "By September 2001, about 3.4 million symptomatic patients had been assessed for tuberculosis, and in the case of nearly 800,000, treatment had been started — in more than half of them, within the previous 12 months."

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## Genomic Medicine

**TO THE EDITOR:** The first case vignette in Guttmacher and Collins's primer on genomic medicine (Nov. 7 issue)<sup>1</sup> is not a good example of the value of genomic medicine; rather, it may be an example of excessive laboratory testing. Heparin prophylaxis during pregnancy would be indicated for Kathleen, the woman described in the vignette, on the clinical basis of her prior estrogen-related deep venous thrombosis, even if she were not heterozygous for the factor V Leiden mutation.<sup>2</sup> Conversely, although she is heterozygous for the factor V Leiden mutation, heparin prophylaxis would not be indicated if she had never had an episode of deep venous

thrombosis.<sup>3,4</sup> Therefore, knowing that she is heterozygous for the factor V Leiden mutation is neither necessary nor sufficient for guiding her clinical care. There may come a time when we can generate an adequately sensitive and specific genomic profile of coagulation, but even then, before ordering a test, we should consider whether the result will have any bearing on the patient's clinical care.

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**THE AUTHORS REPLY:** Weed and Medow raise an interesting point. They are correct in suggesting that the translation of even precise genomic information from the laboratory to the clinic may not always be clear-cut. We certainly agree with their assertion that, absent her history of deep venous thrombosis while taking oral contraceptives, knowledge of Kathleen's factor V Leiden mutation would not indicate a need for heparin prophylaxis and thus would contribute nothing to her care (and would mean extra costs). However, it was because of that history and because of her family history that testing for factor V Leiden was ordered, and we believe that her physician was correct to do so.

Weed and Medow's assertion that heparin pro-

phylaxis is indicated for Kathleen regardless of her genetic status is, however, debatable. A recent multicenter, prospective study of 125 pregnant women with a history of a single episode of deep venous thrombosis found that "the risk of recurrent antepartum venous thromboembolism in women with a history of venous thromboembolism is low, and therefore routine antepartum prophylaxis with heparin is not warranted."<sup>1</sup> It is because of such data that a recent review suggested that "prophylactic heparin is not required [in the antepartum period] among women without a detectable inherited or acquired thrombophilia in whom a previous venous thrombotic event was associated with a non-recurring risk factor."<sup>2</sup> We believe that Kathleen's management illustrates the value, not the excesses, of genomic medicine.

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## Initial Management of Glycemia in Type 2 Diabetes

**TO THE EDITOR:** In his Clinical Practice article (Oct. 24 issue),<sup>1</sup> Nathan states that "although combination therapy with a sulfonylurea (or glitinides) and insulin has been approved for use, I do not recommend it." The author bases his recommendation on the principle that combination therapy should involve agents with different primary modes of action, but often we use agents with the same mode of action but different pharmacokinetic profiles — a clear example being insulin mixtures.

In most patients with type 2 diabetes, sulfonylureas can be viewed as an "endogenous insulin injection." That being the case, the combination of a long-acting insulin such as insulin glargine or a neutral protamine Hagedorn preparation with a glitinide for postprandial control makes perfect sense, and initial studies have been supportive.<sup>2</sup>

Moreover, the recently published United Kingdom Prospective Diabetes Study (UKPDS 57)<sup>3</sup> showed that the addition of insulin in patients with diabetes that is not optimally controlled by sulfo-

nylurea therapy, as compared with insulin alone, leads to better glycemic control (glycosylated hemoglobin, 6.6 percent vs. 7.1 percent; proportion with <7 percent glycosylated hemoglobin, 47 percent vs. 35 percent). This control was achieved with similar weight gain and, more importantly, with a lower incidence of major hypoglycemic episodes. The combination of insulin and sulfonylurea should still be recommended for selected patients.

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