onstrated that this isotype is ineffective in engaging Fc receptors.[5] Although TGN1412 was used at 1/500 of the dose that was used safely in nonhuman primates, increased avidity of the IgG4 Fc region for human Fc receptors may have caused sufficient cross-linking of CD28 to elicit a cytokine storm. Such a hypothesis could be tested experimentally.

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TO THE EDITOR: Sharpe and Abbas suggest that possible differences in the activation requirements of naive T cells and memory T cells could explain the lack of a biologic signal in animals. Another explanation, they say, is a possible difference in the affinity of the anti-CD28 monoclonal antibody for human and primate CD28 molecules. The accompanying article by Suntharalingam et al. does not discuss possible mechanisms of cytokine-storm induction but does note that similar reactions have been observed in previous trials of some antilymphocyte antibodies. A third possibility — distinct from the specificity of the antibody but more consistent with data from previous antibody trials, which also showed cytokine release syndromes — is that cytokine release is induced by the binding of Fc to Fc receptors. Apart from the cytokine release syndromes, such binding would also induce the superactivation of T cells and would explain the immunopathology that is seen.[1]

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THE AUTHORS REPLY: Wise et al. and Colaco note an additional possible mechanism for the cytokine release syndrome, related to Fc-receptor binding. Species differ greatly with respect to the number of Fc-receptor genes and specific cell-type expression patterns. We really do not understand the differences between nonhuman primates and humans with respect to the diversity of Fc receptors, and we lack information to make cross-species comparisons of the binding of human IgG subclasses to Fc receptors in nonhuman primates.[1] There is a need for better models to address these issues. It should be noted that differences in both the antibody subclass and the glycosylation status of the antibody influence the profile of Fc-receptor binding. In addition, human IgG4 has a low level of binding to Fc receptors but is not a nonbinder. Clearly, it is important to consider the nature of the Fc portion of antibodies as they are developed for clinical use as therapeutic agents.[2]

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The State of Primary Care

TO THE EDITOR: In his Perspective article (Aug. 31 issue),[1] Bodenheimer accurately describes the assault on primary care medicine. Insurers deny payment and bureaucrats add onerous record keeping, while the needs of patients increase. We persist only because of the rewards that are documented in the accompanying Perspective article by Woo.[2]

It seems unlikely that macrosystem improvement will occur in the near future. For small

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practices, rhetoric about efficiency and quality produces more problems than solutions. Pay for performance is a good example. In the 1990s, the "golden age" of health maintenance organizations and capitation, my partner and I were the beneficiaries of a bonus. The reward for a 3-month period — during which we earned a score above 95% in patient satisfaction, adhered to prevention guidelines, and provided same-day appointments and evening office hours — was $6.98.

In contrast, microsystem improvement is available now, through reversion to having patients pay for service. Five years ago, my practice stopped participating in all insurance programs with the exception of Medicare.[3] We require no membership fee and adjust for financial hardship. We offer same-day appointments, after-hours coverage, lower overhead, and coordination with specialists. The demand for services from patients led us to add two more physicians to our practice. I offer this optimistic note to other primary care practices.

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TO THE EDITOR: Bodenheimer errs in dismissing international medical-school graduates (IMGs) in a single sentence. With American medical-school graduates showing a decline in interest in primary care residencies and practices, IMGs are increasingly the "safety net," satisfying the staffing needs of practices and community health centers throughout the country.[1] In the 1990s, with an oversupply of physicians a looming fear, some observers advocated a severe restriction in the training of IMGs. With the current undersupply, such action would be untenable.[2]

The IMG migration has been described as a "brain drain," but given the constraints of rigid and suffocating domestic academic atmospheres and poor remuneration in their own countries, IMGs have tended not to return home.[3] This situation appears to be changing, as shown by the trend of outsourcing images for reading by U.S.-trained IMG radiologists in their native countries.[4] As IMGs, we believe that any examination of the future of primary care must involve a more detailed discussion of the role of IMGs and their contributions.

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TO THE EDITOR: Bodenheimer precisely describes the complexities of providing primary care in an environment that is constrained by inadequate reimbursement, an overwhelming scope of practice, and a decreasing number of physicians. He notes that "many nurse practitioners and physician assistants who could join the primary care workforce are instead going to work in wealthier specialty practices." Recent data regarding nurse-practitioner practices do not support this statement.

As is consistent with their role, 85% of nurse practitioners currently practice in primary care.[1,2] Nurse practitioners are more likely than physicians to care for the underserved, work in rural areas, and provide health-promotion services.[2,3] In 2005, schools of nursing enrolled more than 18,000 students in programs for primary care nurse practitioners and graduated more than 5000.[2,4] More than 11,000 of these students were enrolled in programs for family nurse practitioners.[4] In contrast, 1132 graduates of U.S. medical schools enrolled in family medicine residencies in the same year.

Clearly, the paradigm for the provision of primary care services is changing. The dwindling supply of primary care physicians suggests that nurse practitioners may become the future gatekeepers of primary care.

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TO THE EDITOR: In the United States today, there are various kinds of primary care providers, with various levels and types of training. There are also various types of patients: elderly people with multiple chronic, serious conditions; others with dangerous acute illnesses; and healthy people seeking preventive care. There are problems for which self-treatment is suitable (upper respiratory infection, for example) and other conditions (such as obesity) that may be more responsive to public health measures. When we lump all the health problems together as "primary care" and use the same payment method for each, we essentially pay an average: not enough for complex cases and maybe too much for simple ones. Increasing the amount of reimbursement for every visit because an office has an electronic system and ancillary personnel will not fix this problem. We need to restructure the coding system to place greater emphasis on the complexity and number of problems that patients have and less emphasis on the extent of our examination.

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TO THE EDITOR: I know from my personal experience the perilous status of primary care. A student recently remarked to me that students seeking residencies in internal medicine are perceived as being too weak to obtain any other type of residency. Another student requested a letter of recommendation for a radiology residency with an alternative version for use in securing a fallback position in internal medicine. When one internal medicine resident requested an additional day per week of continuity clinic to help prepare for a career in primary care, his peers pressured him to withdraw the request, because they would have had to cover his inpatient responsibilities during those hours.

An increasing shortage of faculty further threatens the discipline. Instruction in physical diagnosis, traditionally performed by internists, is now sometimes directed by anesthesiologists. My own patient panel has had several influxes of new patients as our residency alumni leave primary care and refer their patients back to the training site. Thus, I see both patients whom I inherited from my retired mentors and patients inherited from my prematurely retired trainees.

Let us again foster the social and political movement toward more equitable health care.

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TO THE EDITOR: The country's two largest medical organizations for primary care physicians are working purposefully to answer Bodenheimer's call for a national policy to rescue primary care. The American Academy of Family Physicians and the American College of Physicians have joined together to advocate for a patient-centered medical home based on a patient's continuous relationship with a personal physician. We believe that this model not only is what patients and physicians want but also promises to make health care more effective, more efficient, and more equitable.

However, the success of this model is predicated on macrosystem reform. The patient-centered medical home requires a different way of compensating physicians. Payments should reflect the value of services involved in coordinating care, support practices in acquiring needed information technologies, and reward measurable and continuous quality improvement.

We have a plan to make a patient-centered medical home a reality for all Americans. In return, government and payers must invest in primary care by eliminating a flawed system that rewards fragmented, high-volume, overspecialized, and inefficient care and adopting a payment system that facilitates high-quality and efficient care centered on the relationships of patients with their primary care physicians.

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DR. BODENHEIMER REPLIES: The responses from the correspondents all contribute to a better understanding of the situation of primary care in the United States. Regarding the letter from Das and Moorthi, a detailed examination of IMGs can be found in Mullan's 2005 article in the *Journal*.[1] Poplin wisely suggests that the coding system needs to be restructured in order to focus on the complexity and number of problems that patients have. Many ideas for fixing the coding system or moving away from fee-for-service payment to more blended payment modes have been proposed, and Poplin's proposal is one possibility. The fear is that the coding system will not be reformed and will continue to ignore the increasing intensity of care provided by most primary care practices.

Oserman eloquently describes the distress of training programs for primary care physicians. But not all is dismal. Currents of reform are stirring in residencies in family medicine and general internal medicine, with the potential for making primary care training far more attractive.

The letter from Becker et al. about nurse practitioners brings up an important issue. Until recently, I believed that nurse practitioners would become the primary care clinicians of the future, and having worked with excellent nurse practitioners and physician assistants, I have great confidence in these advanced practice clinicians. The references provided by Becker et al. are compelling. But recently, I have heard many anecdotes of nurse-practitioner graduates who are having difficulty finding jobs in primary care (owing to the unstable finances of many primary care practices) and are opting for positions in cardiology or other specialties. It is too early to tell, but the next few years may show us whether this is the start of yet another trend away from primary care.

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Heparin-Induced Thrombocytopenia

TO THE EDITOR: Arepally and Ortel (Aug. 24 issue)[1] review the role of bivalirudin as one of the therapeutic options in the management of heparin-induced thrombocytopenia. In Table 2 of their article, the activated clotting time is listed as a means of monitoring the anticoagulation profile of bivalirudin. There is no linear correlation between the standard activated clotting time and the plasma bivalirudin concentration.[2,3] Several studies have shown that the standard activated clotting time does not provide an accurate measurement of the anticoagulation effect of bivalirudin, especially at large doses.[3-5] However, there is a good linear relationship between the bivalirudin concentration and the ecarin clotting time,[3] and this test should be considered the test of choice for monitoring the effects of bivalirudin.

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THE AUTHORS REPLY: The activated clotting time is a point-of-care test that was developed for rapid, bedside monitoring of heparin therapy in patients undergoing cardiac catheterization or cardiopulmonary bypass surgery.[1] The ecarin clotting time is a measurement involving the use of ecarin, an enzyme found in snake venom (*Echis carinatus*), which converts prothrombin to meizothrombin. Meizothrombin, an intermediary thrombin derivative,[2] is particularly sensitive to inactivation by direct thrombin inhibitors. As noted by Saad, the ecarin clotting time is more closely correlated with bivalirudin levels (r=0.9) than is the activated clotting time (r=0.7).[3] Commercial ecarin-clotting-time assays, however, are generally limited to reference laboratories and are not available in

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