

THE AUTHOR REPLIES: Zerbini and colleagues are correct about the discrepancy in referring to endothelial progenitor cells as “CD45⁺” versus “CD45dim.”¹ It is not uncommon for some investigators to use these terms interchangeably, as I have, and to sometimes describe these cells as CD45⁻ (e.g., in a report by Alvarez et al.³) and sometimes as CD45dim (e.g., in a report by Duda et al.⁴). However, partly on the basis of data in the figure presented by Zerbini and colleagues, the point is made that these cells are phenotypically distinct, thus calling for a more precise definition when referring to endothelial progenitor cells. I agree. Whether endothelial progenitor cells are CD45dim in all cases cannot be said with certainty at present, which highlights the problem of an accepted standard definition of endothelial progenitor cells based especially on expression of cell-surface markers but also on functional criteria. An international consensus workshop is needed to make recommendations regarding such a

standard definition, given the importance of endothelial progenitor cells in cancer and cardiovascular disease. It is also reassuring that the data of Bertolini and colleagues² showing that human endothelial progenitor cells have a CD45dim-CD34+VEGFR-2+CD133+ phenotype were confirmed.

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1. Kerbel RS. Tumor angiogenesis. *N Engl J Med* 2008;358:2039-49.
2. Bertolini F, Shaked Y, Mancuso P, Kerbel RS. The multifaceted circulating endothelial cell in cancer: towards marker and target identification. *Nat Rev Cancer* 2006;6:835-45.
3. Alvarez DF, Huang L, King JA, ElZarrad MK, Yoder MC, Stevens T. Lung microvascular endothelium is enriched with progenitor cells that exhibit vasculogenic capacity. *Am J Physiol Lung Cell Mol Physiol* 2008;294:L419-L430.
4. Duda DG, Cohen KS, Scadden DT, Jain RK. A protocol for phenotypic detection and enumeration of circulating endothelial cells and circulating progenitor cells in human blood. *Nat Protoc* 2007;2:805-10.

Pursuit of an Expanded Physician Supply

TO THE EDITOR: In his Health Policy Report on physician supply, Iglehart (April 17 issue)¹ focuses on a result of the Medicare Payment Advisory Commission (MedPAC) 2006 survey of Medicare beneficiaries: among a small percentage of beneficiaries who were seeking a new specialist, more of them had a problem finding one in 2006 than in 2004. This finding must be considered in context. Each year, beneficiaries who respond to our survey report having better access to specialists than to primary care physicians. That was the result again in 2007, when 85% of those seeking a new specialist reported having had no problem, as compared with 70% of those seeking a new primary care physician.² Moreover, MedPAC is concerned that primary care services are undervalued in Medicare's physician fee schedule and are at risk of being underprovided relative to procedurally based services. In response, MedPAC recently recommended increases in fee-schedule payments for primary care services that are “furnished by practitioners focused on delivering primary care” and a medical home pilot program in Medicare.³ These recommendations are in addition to reforms MedPAC recommended previously

to better address overvalued services in the fee schedule.⁴

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1. Iglehart JK. Grassroots activism and the pursuit of an expanded physician supply. *N Engl J Med* 2008;358:1741-9.
2. Medicare Payment Advisory Commission. Report to the Congress: Medicare payment policy. March 2008. (Accessed July 25, 2008, at http://www.medpac.gov/chapters/Mar08_Ch02b.pdf)
3. *Idem*. Report to the Congress: reforming the delivery system. June 2008. (Accessed July 25, 2008, at http://www.medpac.gov/documents/Jun08_EntireReport.pdf)
4. *Idem*. Report to the Congress: Medicare payment policy. March 2006. (Accessed July 25, 2008, at http://www.medpac.gov/documents/Mar06_EntireReport.pdf)

TO THE EDITOR: Iglehart leaves out one factor that impinges on physician supply: the number of applicants to medical school. The number relative to positions has gradually fallen over the years. When I applied to medical school in 1942, some schools received as many as 10 applications for every position. The current ratio of applicants to acceptances is approximately 2:1.^{1,2} If this trend continues, quality will eventually decrease, and it is possible that later there won't be enough qual-

ified applicants to fill available positions. Why do we have so few applicants? Medicine is no longer attractive to our youngsters, and the best ones are training in other fields. The reasons for this are multiple and need to be addressed by necessary measures, including proper health care reform.

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1. Blumenthal D. New steam from an old cauldron — the physician-supply debate. *N Engl J Med* 2004;350:1780-7.
2. Mullan F. The case for more U.S. medical students. *N Engl J Med* 2000;343:213-7.

TO THE EDITOR: Although Iglehart's article captures the medical community's collective pursuit of an expanded physician supply, it should be noted that the expansion of medical schools does more than heal a town's lackluster economy. It provides some communities that are faced with limited access to physicians much-needed health care.

The osteopathic medical profession has a tradition of producing primary care physicians who will practice in rural and other medically underserved communities. Many colleges of osteopathic medicine have focused on meeting the needs of underserved rural and urban populations.¹

Since physicians are likely to practice within the area where they received their training, new colleges of osteopathic medicine are being established in some of the nation's most medically underserved regions, including New York City's Harlem community, which welcomed its inaugural class of osteopathic medical students last fall. As the osteopathic medical community looks toward future growth, it will continue to honor its tradition of producing primary care physicians to ensure that all people have access to health care.

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1. Levitan T. AACOM projections for growth through 2012: results of a 2007 survey of US colleges of osteopathic medicine. *J Am Osteopath Assoc* 2008;108:116-20.

THE AUTHOR REPLIES: Hackbarth has a valid point with which I do not quibble. I would note that MedPAC, which he chairs, has pledged to examine physician-workforce issues more closely, "especially with respect to the supply of primary care providers" and "the choices medical students and

residents make about their career specialty."¹ I favor a more thorough examination of the subject or, as Brennan called for recently, a federally supported "comprehensive study of the adequacy of the current physician workforce and projected future needs."²

The number of applicants to medical schools has fluctuated widely over the years, as Haddy points out. However, 2007 marked the fifth straight year of growth in the number of applicants to allopathic schools, increasing from 33,625 in 2002 to 42,315 in 2007. In the same 5-year period, applications to colleges of osteopathic medicine increased from 6324 to 11,459. Perhaps the most relevant question is whether there will be an adequate number of applicants to medical schools and colleges of osteopathy to treat the health care needs of a U.S. population that increases by about 25 million people every decade. The Association of American Medical Colleges (AAMC), which has recommended that allopathic schools increase their class sizes by 30% to accommodate this growing population, believes so. The AAMC concluded recently, "We believe future applicant pools should be large enough to sustain a national first-year medical school enrollment of 21,434 students, equal to a 30% increase over the matriculating class of 2002."³

Ajluni is correct in saying that doctors of osteopathic medicine have established practices in medically underserved communities more frequently than have their colleagues in allopathic medicine. However, new graduates of schools of osteopathic medicine are attracted to these locales and careers in primary care less frequently than in the past and are turning increasingly to specialization. According to annual surveys of graduating seniors that were conducted by the American Association of Colleges of Osteopathic Medicine, the number of students planning to pursue careers in primary care dropped from 43.8% in 1999 to 28.3% in 2007. Many medical students are turning to non-primary care specialties because of both higher pay and more lifestyle-friendly working conditions. In 1999, students of osteopathic medicine reported having a mean educational debt of \$116,700; by 2007, that number had reached \$168,031. By comparison, on the basis of responses to AAMC questionnaires, students of allopathic medicine reported having a mean educational debt of \$76,141 in 1999 and \$139,500 in 2007.

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1. Report to the Congress: Medicare payment policy. Washington, DC: Medicare Payment Advisory Commission, March 2007. (Accessed July 25, 2008, at http://www.medpac.gov/documents/030107_Testimony_Mar07_report.pdf.)
2. Iglehart JK. Grassroots activism and the pursuit of an expanded physician supply. *N Engl J Med* 2008;358:1741-9.
3. Garrison G, Matthew D, Jones RF. Analysis in brief: future medical school applicants. 1. Overall trends. Analysis in brief. Vol. 7. No. 3. Washington, DC: Association of American Medical Colleges, May 2007:1-2.

Glucagon-like Peptide 1–Receptor Scans to Localize Occult Insulinomas

TO THE EDITOR: The precise localization of some insulinomas (islet-cell adenomas that secrete insulin) with the use of conventional imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), endosonography,¹ and indium-111 (¹¹¹In)–labeled pentetreotide scintigraphy (OctreoScan),² is a challenging clinical problem. In vitro studies have demonstrated that receptors for glucagon-like peptide 1

(GLP-1) are highly overexpressed in almost all insulinomas.^{3,4} Therefore, GLP-1-like radioligands retaining high binding affinity to GLP-1 receptors have been developed. One such radioligand, [Lys⁴⁰(Ahx-DTPA-¹¹¹In)NH₂]exendin-4, successfully targeted insulinomas in the Rip1-Tag2 mouse.⁵ We evaluated the diagnostic value of GLP-1–receptor scintigraphy in two patients with insulinomas that either were not localized (Patient 1) or were

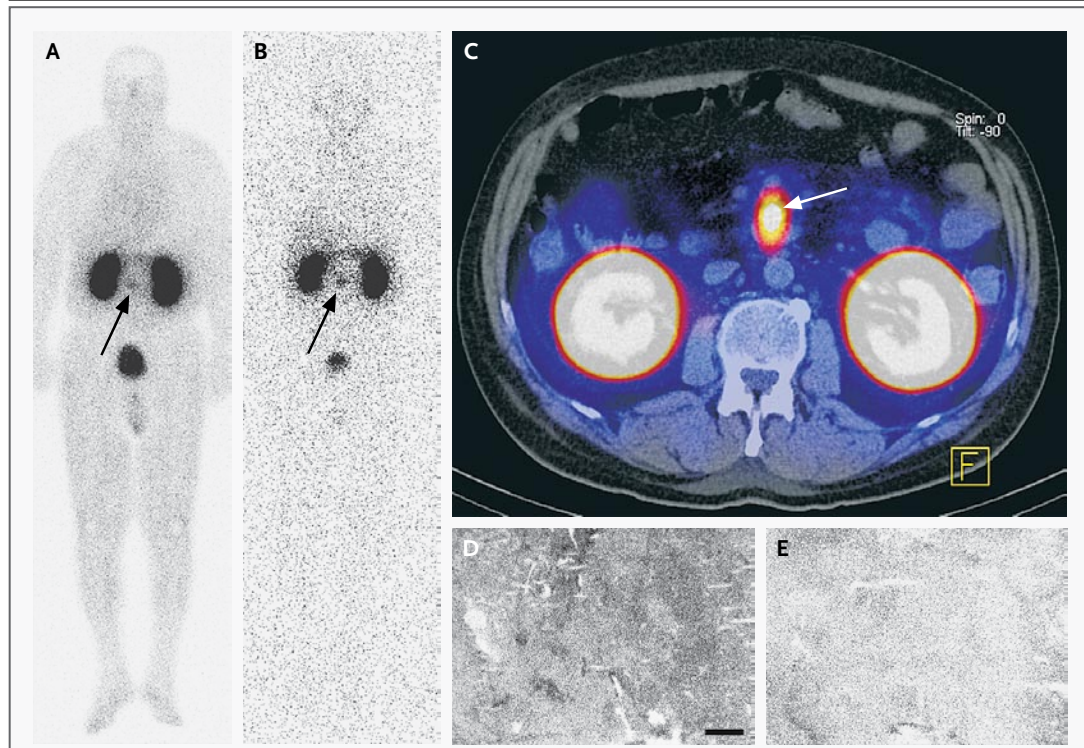


Figure 1. GLP-1–Receptor Imaging of an Insulinoma in Patient 1.

In Patient 1, a 64-year-old man with symptomatic neuroglycopenia and biochemically confirmed endogenous hyperinsulinism, whole-body planar scans show an insulinoma (arrow) with a tumor-to-background ratio of 5.8 at 4 hours after injection of a radioligand (Panel A) and of 13.4 at 4 days after injection (Panel B). Because of urinary excretion of the radioligand, the kidney and bladder labeling are less prominent on day 4 than at 4 hours, so late scans (2 to 4 days after injection) are recommended. Transaxial single-photon-emission CT (SPECT) that was performed 4 days after the injection of a radioligand shows uptake in a small nodule between the duodenum and the superior mesenteric artery (Panel C, arrow). A glucagon-like peptide 1 (GLP-1)–receptor autoradiograph shows total binding of iodine-125–labeled GLP-1(7-36) amide in tumor tissue (Panel D); an autoradiograph with nonspecific binding is shown for comparison (Panel E). The bar represents 1 mm.