

athy of lumbar spinal stenosis from peripheral neuropathy. We are not aware of data indicating that the severity of electrodiagnostic findings can be used to identify whether radiculopathy or co-existing neuropathy is the most symptomatic process in a patient who has both disorders.

Rhon points to a randomized trial that was not included in our review. This study shows the efficacy of manual physical therapy in conjunction with a treadmill-walking program with body-weight support as compared with flexion exercises and the treadmill-walking program. These promising findings merit further investigation.

Our 1995 report on the sensitivity and specificity of medical-history and physical findings in patients with spinal stenosis¹ identified wide-based gait, in which patients walk with their feet separated by a greater-than-usual distance, as a

sign that is insensitive (present in 43% of patients with stenosis) but specific (absent in 91% of patients without stenosis) and that helps to distinguish lumbar spinal stenosis from other sources of back pain. As van Gijn suggests, further work on the reliability and validity of this and other medical-history and physical findings would be a welcome addition to the literature. We appreciate van Gijn's clarification regarding the presence of descending nerve roots, rather than the posterior column (spinal cord), at the lower lumbar levels.

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More on Ovarian Insufficiency with Imatinib

TO THE EDITOR: Christopoulos et al. (March 6 issue)¹ report a case of primary ovarian insufficiency associated with imatinib. Although the data provided are suggestive of primary ovarian insufficiency, the cause-and-effect relationship is speculative, not reaching the "probable" level on an objective causality-assessment scale.² It is noteworthy that fertility in female rats is not adversely affected by imatinib, and pregnancy in women taking imatinib has occurred.^{3,4} Also, despite the expanding use of imatinib, no other cases of primary ovarian insufficiency have been reported. All these facts, along with the presence of follicles in the patient's ovaries on ultrasonography and the delay in the development of her amenorrhea, are inconsistent with the proposed mechanism and with the understanding of toxicant-induced apoptosis of female germ cells.⁵ Moreover, alternative etiologic factors, including other exposures, were not addressed, and the possibility of spontaneous, karyotypically normal primary ovarian insufficiency — a largely idiopathic condition in which ovarian function is generally intermittent and unpredictable — was not systematically ruled out. This finding may well be a chance association, and only careful, long-term evaluation of patients receiving imatinib can determine its validity.

The views expressed in this letter are those of the authors and do not constitute an official position of the Department of Health and Human Services.

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THE AUTHORS REPLY: The Naranjo probability scale referred to by Malozowski et al. was recently reported to lack reproducibility and have a poor

negative predictive value.¹ It should be noted that plasma levels of imatinib in patients given high doses of the drug exceed those of the no-effect level in the study of rat fertility. We also disagree with the specific reservations expressed by the correspondents. The time relationship was reasonable, with oligomenorrhea occurring a few months after the increase in the dose of imatinib. There were no other exposures, and no alternative causes were found on routine investigation of amenorrhea. Finally, the hypothesis of an etiologic link between imatinib and ovarian insufficiency is biologically plausible, since pathways involving kinases targeted by imatinib appear to play critical roles in the survival and maturation of follicles and oocytes.²⁻⁴

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Propranolol for Severe Hemangiomas of Infancy

TO THE EDITOR: Despite their self-limited course, infantile capillary hemangiomas can impair vital or sensory functions or cause disfigurement. Corticosteroids are the first line of treatment for problematic infantile capillary hemangiomas^{1,2}; other options include interferon alfa³ and vincristine.⁴ We have observed that propranolol can inhibit the growth of these hemangiomas. Our preliminary data from 11 children are summarized in Table 1 in the Supplementary Appendix, available with the full text of this letter at www.nejm.org.

The first child had a nasal capillary hemangioma. Despite corticosteroid treatment, the lesion was stabilized but obstructive hypertrophic myocardiopathy developed, so the patient was treated with propranolol. The day after the initiation of treatment, the hemangioma changed from intense red to purple, and it softened. The corticosteroids were tapered, but the hemangioma continued to improve. When the corticosteroids were discontinued, no regrowth of the hemangioma was noted. When the child was 14 months of age, the hemangioma was completely flat.

The second child had a plaque-like infantile capillary hemangioma involving the entire right upper limb and part of the face (Fig. 1). At 1 month of age, a subcutaneous component developed, and despite corticosteroid treatment, the hemangioma continued to enlarge. Magnetic resonance imaging revealed intraconal and extra-

conal orbital involvement, as well as an intracervical mass causing compression and tracheal and esophageal deviation (see the Supplementary Appendix). Ultrasonography showed increased cardiac output, and treatment with propranolol, at a dose of 2 mg per kilogram of body weight per day, was initiated. Seven days later, the child was able to open his eye spontaneously, and the mass near the parotid gland was considerably reduced in size. Prednisolone was discontinued at 4 months of age, without any regrowth of the hemangioma; at 9 months of age, the eye opening was satisfactory, and no major visual impairment was noted.

After written informed consent had been obtained from the parents, propranolol was given to nine additional children who had severe or disfiguring infantile capillary hemangiomas (see Table 1 in the Supplementary Appendix). In all patients, 24 hours after the initiation of treatment, we observed a change in the hemangioma from intense red to purple; this change was associated with a palpable softening of the lesion. After these initial changes, the hemangiomas continued to improve until they were nearly flat, with residual skin telangiectasias. Ultrasound examinations in five patients showed an objective regression in thickness associated with an increase in the resistive index of vascularization of the hemangioma (Table 1 in the Supplementary Appendix).