tainty, the risks of treatment weighed against the potential benefits of further testing, and the leading hypothesis being pursued were all suggested as salient variables for the selection of tests. Another variable mentioned was the difference between a hypothetical case and an actual patient. We want to share results from a survey suggesting that this last variable may be a major explanation for the differences between the liberal tester and the parsimonious tester.

One of us saw a 46-year-old man who had a two-year history of burning midepigastric pain relieved by food. Examination demonstrated only a grade 1/6 aortic-insufficiency murmur. The results of laboratory tests were normal except for an alanine aminotransferase level of 89 IU per liter (normal, 0 to 60). Three years earlier the alanine aminotransferase level had been 30 IU per liter. A decision was made to reexamine the patient's liver function in six months on the basis of published recommendations[1] and data that 84 percent of results of single tests of liver function showing elevations are falsely positive.[2] He was referred to a gastroenterologist for upper gastrointestinal endoscopy, which revealed duodenitis, an active duodenal ulcer, and no evidence of *Helicobacter pylori*. The gastroenterologist ordered a battery of additional laboratory tests costing $384 to evaluate further the alanine aminotransferase level.

Noting the additional testing, we hypothesized that this represented an example of more expensive specialty care as compared with less expensive primary care and designed a survey to test this. Academic and practicing general internists and gastroenterologists were sent this case report and a list of tests that could be used to evaluate the alanine aminotransferase level further.

To our surprise, specialists and generalists alike indicated they would wait six months, repeat the alanine aminotransferase measurement, or perform only liver-function tests initially. The gastroenterologist who actually treated the patient, when faced with this hypothetical case, ordered only repeated liver-function tests ($61) and indicated that he would delay further testing. This small experience suggests that when faced with a hypothetical case, physicians may find diagnostic uncertainty easier to accept and will carefully consider reasons for ordering tests. In practice, diagnostic uncertainty may be less palatable, and as a consequence, physicians may be more liberal testers. Although we present as evidence the responses of only one person, this interesting dichotomy may help explain some of the differences noted by Putterman and Ben-Chetrit. What we say we would do and what we actually do in clinical problem-solving may differ.

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To the Editor: The insightful discussion by Drs. Putterman and Ben-Chetrit points out the importance of remembering analytic probability before one orders any test. I was dismayed, however, to see the misuse of the serum CA-125 test as a screen for ovarian cancer. The pelvic and rectal examinations were known to be normal, and in a post-menopausal woman, the diagnostic yield for cancer is low for this test.

An additional cause for dismay is the statement that the elevated CA-125 level was assumed to be a false positive result. I believe rather that it was a true positive value for an alternative diagnosis. Several studies, including some of the original ones by Bast and colleagues, identified the presence of this antigen in pleural and peritoneal lining cells.[1,2] Several other case reports and clinical studies have documented the increase in CA-125 levels in a variety of benign situations such as ascites, menstruation, and other inflammatory or infiltrative processes involving the mesothelium.[2-4] Eosinophilic gastroenteritis should probably be added to the list of diagnostic entities to be considered when the CA-125 is increased.

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To the Editor: In the Clinical Problem-Solving article by Putterman and Ben-Chetrit, the discussant and the authors question the extent of the workup necessary in cases of very high levels of eosinophilia. Moreover, they all dismiss the diagnosis of eosinophilic leukemia, because all the eosinophils in a complete blood count were mature. Recently, we treated a patient for idiopathic hypereosinophilic syndrome that was later found to be eosinophilic leukemia.

A 39-year-old woman presented with a one-week history of a high fever, cough, myalgia, chest pain, and swelling of the eyelids. She had never traveled outside Europe. Physical examination was normal except for tenderness of the right upper quadrant. A complete blood count was normal except for findings of 71 percent eosinophils, all mature. The absolute eosinophil count was 35,540 per cubic millimeter. The erythrocyte sedimentation rate was 40 mm per hour. Other studies showed only a moderate abnormality of liver function. Stool microscopy detected no ova or parasites. Enzyme-linked immunosorbent assays for fasciola, echinococcus, taenia, toxocara, strongyloides, and trichinella were negative. The serum IgE level was normal. A test for antinuclear antibodies and rheumatoid factor was negative. A chest x-ray film showed patchy pulmonary infiltrates and a questionable left pleural effusion. An abdominal ultrasound examination revealed no abnormalities except for the presence of cholelithiasis. A computed tomographic scan of the sinuses revealed no abnormalities. A bone marrow biopsy showed massive numbers of eosinophils whose development was normal and first-degree fibrosis on the Bauermeister scale. A flow cytometric evaluation of the bone marrow did not detect abnormal populations. A diagnosis of hypereosinophilic syndrome was made, and the patient was treated with amoxicillin, mebendazole, and prednisone. The fever, cough, and myalgia disappeared within days. The eosinophil count dropped to 2370 per cubic millimeter after two weeks, and the pulmonary infiltrates disappeared.

Serologic tests for helminths remained negative. However, symptoms and eosinophilia returned after corticosteroid therapy was stopped. Cytogenetic analysis of the bone marrow unexpectedly showed 30 of 30 cells in mitosis to have an ab-

normal karyotype: 46,XX,t(9;16)(q34;p13.1), indicating that the correct diagnosis was eosinophilic leukemia.

We conclude that the presence of mature eosinophils does not exclude the possibility of an eosinophilic leukemia and that the diagnosis of the idiopathic hypereosinophilic syndrome should not be made too early.

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The authors reply:

To the Editor: Van den Ende et al. suggest that our patient may have had eosinophilic leukemia rather than idiopathic hypereosinophilic syndrome. Indeed, as discussed in the excellent review by Weller and Bubley[1] cited in our paper, the distinction between eosinophilic leukemia and hypereosinophilic syndrome may be quite difficult to make in some patients. Although cytogenetic analysis was not performed on our patient, chromosomal abnormalities can also occur in hypereosinophilic syndrome.[1] The absence of other leukemic features and the clinical course in the months since the diagnosis do not support the hypothesis of a malignant cause of her disease at this time.

Dr. Lokich and Dr. Hassell disagree with the steps taken by the primary physician to exclude a diagnosis of cancer. Dr. Lokich suggests that had cancer been found in this patient, it would probably have been "incurable and untreatable." We cannot speak for the primary physician (the liberal tester) who chose the specific diagnostic workup; however, we think that confirming a diagnosis of a neoplastic disorder has crucial implications for the patient, even if the disease is not curable with available therapies. The clinical adage that an uncommon manifestation (eosinophilia) of a common disease (cancer) occurs more frequently than a common manifestation of an uncommon disease (hypereosinophilic syndrome) may also have played a part in the formulation of the diagnostic plan. The elevation in the CA-125 level could have been a true positive result for an alternative diagnosis, as pointed out by Dr. Hassell. However, for the purposes of the patient's physicians (and similarly for other physicians who commonly use tumor markers to screen for cancer), the high level of CA-125 was a false positive result that no doubt contributed to a further extension of the diagnostic search.

The preliminary results of the survey conducted by Drs. Kreger and Murden are interesting. Indeed, it would seem to be the experience of many physicians that when they are faced with a critically ill patient in practice, diagnostic uncertainty suddenly becomes much less palatable than when the same patient is discussed in a hypothetical context. We agree with Drs. Kreger and Murden that this dichotomy may explain some of the observed differences between the attending physicians and the discussants in the Clinical Problem-Solving feature.

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HERPESVIRUS-LIKE DNA SEQUENCE IN ANGIOSARCOMA IN A PATIENT WITHOUT HIV INFECTION

To the Editor: Recent studies have demonstrated the presence of a new gamma herpesvirus–like DNA sequence, designated Kaposi's sarcoma–associated herpesvirus (KSHV) or human herpesvirus-8, in different forms of Kaposi's sarcoma in patients infected with the human immunodeficiency virus (HIV)[1] and in uninfected patients.[2] KSHV sequences were also detected in proliferative lesions other than Kaposi's sarcoma (AIDS-related body-cavity–based lymphomas,[3] Castleman's disease,[4] and various proliferative skin lesions[5]) in immunocompromised patients. Nador et al. (Oct. 5 issue)[6] reported finding KSHV DNA in a body-cavity–based lymphoma in an HIV-negative patient. We report detecting the KSHV sequence in another non–Kaposi's sarcoma tumor from a nonimmunocompromised patient.

A 63-year-old woman presented with a one-year history of a small, reddish-blue discoloration of the skin on her right cheek, resembling a hematoma, that had developed into a rapidly growing angiomatous tumor two weeks before admission. The patient was HIV-negative, had not received any immunosuppressive therapy, and had no clinical signs of immunodeficiency. After radical excision of the tumor, the clinical diagnosis of angiosarcoma was confirmed by histologic examination.

DNA was extracted from the paraffin-embedded tissue, and the sample was tested for the presence of KSHV sequences by the polymerase chain reaction (PCR) with primers specific for the 233-base-pair (bp) $KS330_{233}$ fragment, as described previously.[1,2] The results are shown in Figure 1. The 233-bp amplification product was identified in the angiosarcoma sample, as well as in a sample of Kaposi's sarcoma from an HIV-negative patient. The specificity of the band was confirmed by hy-

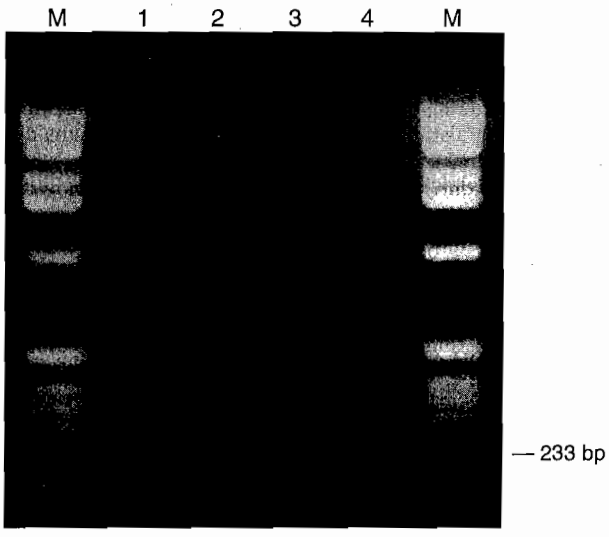

Figure 1. PCR Amplification of KSHV DNA with $KS330_{233}$ Primers. The 233-bp amplification products were detected in the angiosarcoma tissue (lane 2), as well as in a sample of tumor tissue from an HIV-negative patient with Kaposi's sarcoma (lane 3), but not in samples of sterile water (lane 1) or tumor tissue from an HIV-negative patient with basal-cell carcinoma (lane 4). M denotes the molecular-weight marker.