patients who underwent a baseline bone marrow evaluation at the time of diagnosis; in 21 of these patients (3.2%), the percentage of bone marrow plasma cells was at least 60%. The median time to progression to symptomatic myeloma was significantly shorter among the patients with 60% or more bone marrow involvement, as compared with those having less than 60% involvement (P<0.001) (Fig. 1). Progression to myeloma occurred within 2 years of the diagnosis in 95% of the patients with 60% or more bone marrow plasma cells, with a median time to progression of 7 months (95% CI, 1.0 to 12.9). We conclude that the natural history of SMM is based almost exclusively on data from patients in whom the number of bone marrow plasma cells is less than 60%. In patients without end-organ damage at diagnosis but with 60% or greater bone marrow involvement, the clinical course is characterized by progression to symptomatic myeloma within 2 years. Such patients should be considered to have myeloma that requires therapy at the time of diagnosis.

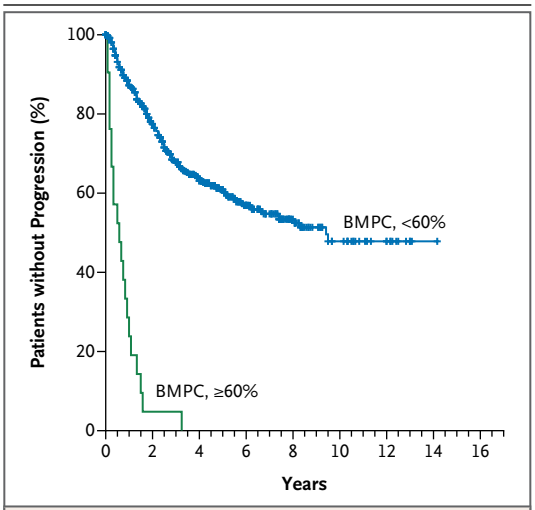

Figure 1. Time to Progression of Disease in Patients Diagnosed with Smoldering Multiple Myeloma, as Stratified According to the Percentage of Plasma Cells in the Bone Marrow (BMPC) at Baseline.

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Disclosure forms provided by the authors are available with full text of this letter at NEJM.org.

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The TEMPI Syndrome — A Novel Multisystem Disease

TO THE EDITOR: The description of a man with erythrocytosis and perinephric fluid collections recently appeared in the Case Records of the Massachusetts General Hospital[1] (Patient 1 in Table 1), and the authors of that article appealed to readers to share similar cases. Two additional patients were identified (Patients 2 and 3), and a review of the literature identified three more patients with similar findings[2-4] (Patients 4, 5, and 6). These six patients shared five characteristics — telangiectasias, elevated erythropoietin level and erythrocytosis, monoclonal gammopathy, perinephric-fluid collections, and intrapulmonary shunting — defining a syndrome that we have termed the TEMPI syndrome.

The four men and two women presented between the ages of 35 and 56 years. In the three patients for whom we have longitudinal follow-up, the symptoms have been slowly and steadily progressive. Telangiectasias developed over the face, trunk, and arms. Increases in serum erythropoietin levels, which eventually reached values exceeding 5000 mU per milliliter, preceded the intrapulmonary shunting and the development of hypoxemia. Sampling of the perinephric fluid revealed a clear, aseptic, serous fluid having low levels of protein, few leukocytes, and no cholesterol or triglycerides. In the four patients tested, serum protein electrophoresis revealed an IgG monoclonal gammopathy of approximately 0.7 g per deciliter (with an associated kappa light chain in all three patients tested). Bone marrow biopsies revealed less than 10% plasma cells, consistent with a monoclonal gammopathy

Table 1. Characteristics of Patients with the TEMPI Syndrome.*

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Demographic						
Age (yr)	42	36	39	35	56	36
Sex	Male	Female	Female	Male	Male	Male
Year of presentation	2001	2005	1991	1978	1970	2002
Geographic location	Memphis, TN	Antwerp, Belgium	Los Angeles	Manchester, U.K.	Seattle	Indianapolis
Race or ethnic group	White	Belgian	Indian	White	Finnish	Mexican
TEMPI syndrome						
Telangiectasias, most prominent over the face, trunk, arms, and hands	Yes	Yes	Yes	NR	Yes	NR
Erythrocytosis	Yes	Yes	Yes	Yes	Yes	Yes
Hematocrit at presentation (%)	58	64	58	62	66	73
Erythropoietin (mU/ml)						
First measurement	16	50	600	NR	Increased	38
Highest value	>5000	>5000	>5000	>500	Increased	NR
Monoclonal gammopathy	IgG kappa	IgG kappa	IgG kappa	NR	IgG	NR
MGUS	Yes	Yes	Yes	NR	NR	NR
Perinephric fluid between the kidney and the renal capsule, without parenchymal renal cysts	Yes	Yes	Yes	Yes	NR	Yes
Requiring surgical marsupialization	Yes	No	Yes	Yes	No	Yes
Intrapulmonary shunting, microscopic	Yes	Yes	Yes	NR	Yes	NR
Hypoxemia	Yes	Yes	Yes	NR	Yes	Yes
Other						
Venous thrombosis†	Yes	Yes	Yes	NR	NR	NR
Spontaneous intracranial hemorrhage	No	Yes	Yes	NR	NR	NR

* Race or ethnic group was reported by the investigators. MGUS denotes monoclonal gammopathy of unknown clinical significance, and NR not reported.

† Thrombosis involved the internal jugular vein in Patient 1, the cerebral venous sinus in Patients 2 and 3, and the common femoral vein in Patient 3.

of unknown significance. Three patients suffered spontaneous venous thromboses, and two have had spontaneous intracranial hemorrhages without identifiable arteriovenous malformations.

Despite extensive imaging and testing, the pathophysiology underlying this syndrome remains unclear. The presence of an IgG kappa paraprotein in all three patients tested may suggest a pathogenic role of the paraprotein.

Trials of immunomodulatory agents (thalidomide in Patient 2), anti–vascular epithelial growth factor therapy (bevacizumab in Patient 2), and immunosuppressive agents (sirolimus in Patient 1) were not effective. Treatment of Patient 2 with the proteasome inhibitor bortezomib (8 cycles, 4 doses of 1.3 mg per square meter of body-surface area per cycle) resulted in the disappearance of telangiectasias, normalization of the serum erythropoietin level, eradication of the monoclonal gammopathy, resolution of the perinephric-fluid collection, and a decrease in the intrapulmonary shunting. This dramatic response supports the hypothesis that the IgG kappa paraprotein is involved in the pathophysiology of TEMPI syndrome.

Our patients underwent extensive testing to evaluate their undiagnosed medical condition, and we are grateful to them and to the physicians who participated directly and indirectly in their care. We suspect that other, similar patients exist, and

we would welcome any reader insights, with the goal of uncovering the physiological basis of this new disease.

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INSTRUCTIONS FOR LETTERS TO THE EDITOR

Letters to the Editor are considered for publication, subject to editing and abridgment, provided they do not contain material that has been submitted or published elsewhere. Please note the following:

- Letters in reference to a *Journal* article must not exceed 175 words (excluding references) and must be received within 3 weeks after publication of the article.
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- A letter can have no more than five references and one figure or table.
- A letter can be signed by no more than three authors.
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CORRECTIONS

Early-Childhood Membranous Nephropathy Due to Cationic Bovine Serum Albumin (June 2, 2011;22:2101-10). The affiliations (page 2101) should have read, "From INSERM, Unite Mixte de Recherche Scientifique 702, Université Pierre et Marie Curie . . ." rather than, "From Université Pierre et Marie Curie . . . ." We regret the error. The article is correct at NEJM.org.

Cardiac Arrest in Public versus at Home (April 28, 2011;364:1674-6). In the third letter to the Editor (page 1675), beginning "Many questions . . . ," the second sentence should have read, "The widespread awareness and acceptance of CPR are the product of national ignorance of its downside, majority prevalence of permanent brain damage outcomes among the 8.4% of cardiac arrest victims who do survive CPR (about 25,000 each year)," rather than ". . . national ignorance of CPR's downside: the broad range of outcomes of permanent brain damage among 8.4% of the 25,000 who survive each year." We regret the error. The article is correct at NEJM.org.

NOTICES

Notices submitted for publication should contain a mailing address and telephone number of a contact person or department. We regret that we are unable to publish all notices received. Notices also appear on the Journal's *Web site (NEJM.org/medical-conference). The listings can be viewed in their entirety or filtered by specialty, location, or month.*

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The meeting will be held in Tel Aviv, Israel, Oct. 31 and Nov. 1.

Contact the Secretariat, 7th International Meeting on Intensive Cardiac Care, P.O. Box 574, Jerusalem 91004, Israel; or call (972) 2 6520574; or fax (972) 2 6520558; or see http://www.isas.co.il/cardiac-care2001; or e-mail conventions@isas.co.il.

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