

trials, study subjects would be far better served by centralization of the responsibility for the protection of human subjects than by reliance on an inefficient and sometimes ineffective system in which multiple IRBs duplicate each other's efforts in performing this function. It is implausible to assume that each local IRB at an institution involved in a multicenter trial can amass the expertise and make the time commitment required to maximize the protection of human subjects in the way that a central IRB (or data and safety monitoring board) specifically constituted for this purpose can do. This is not to say that the local IRB should have no role; rather, its responsibility should relate to the conduct of the trial at its site, including consideration of the capabilities of the investigators and any potential conflicts. It is time for the OHRP to recognize that a bet-

ter process is needed for the protection of human subjects in multicenter trials, rather than merely dictate that IRBs must carry out their regulatory obligations.

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1. Steinbrook R. Trial design and patient safety — the debate continues. *N Engl J Med* 2003;349:629-30.
2. Borror K, Carome MA. Human research subject protections under federalwide assurance (FWA) 3136, multiple project assurances (MPA) M-1331, M-1363, and M-1338 and the OHRP-approved assurances for all ARDS Network institutions. Letter to Ronald S. Newbower, Massachusetts General Hospital, Lee E. Limberd, Vanderbilt University, and Robert Kay, the Cleveland Clinic Foundation. Rockville, Md.: Office for Human Research Protections, July 3, 2003. (Accessed October 29, 2003, at http://ohrp.osophs.dhhs.gov/detrm_lettrs/YR03/jul2003.htm.)

Excess Rate of In-Hospital Death in Lyons, France, during the August 2003 Heat Wave

TO THE EDITOR: We report descriptive data on mortality at the Edouard Herriot Hospital in Lyons, France, during the heat wave that lasted in France from August 1 to August 19, 2003. Figure 1 depicts the absolute daily number of in-hospital deaths during the summers of 2002 and 2003 and the corresponding maximal temperatures. During the heat wave, the average temperature was 35.7°C; it was 25.1°C during the same period in 2002.

The Institut de Veille Sanitaire conducted a national survey between August 8 and August 19, 2003, to count the number of heat-related deaths, defined as exposure to hot weather, a body temperature of 40.6°C or higher, and an absence of other causes of hyperthermia. A total of 73 patients died at our hospital during the national survey, as compared with 23 during the same period in 2002; 30 of these 73 patients (41 percent) died from heat-related conditions according to the definition. The median age of these 30 patients was 85 years (range, 54 to 99), and more than 80 percent were older than 75; the ratio of men to women was 0.76. The median body temperature was 41.5°C (maximum, 43.3°C). Fourteen of the patients lived at home (including 5 who lived alone), and 11 lived in a long-term care facility; information on the housing situation for the other 5 patients was not available. The median length of stay between admission and death was one day (range, one to five) among the 21 persons (70 percent) who died from heat-relat-

ed conditions after admission through the emergency department.

Excess rates of heat-related deaths have been reported elsewhere.¹⁻⁴ We report a quantifiable increase in mortality with the heat wave in France in August 2003. These data need to be reanalyzed on an annual basis and compared with data from previous years. A heat wave may accelerate death for some patients without having an effect on the annual mortality rate.

Most of the patients who died were older than 80 years. Factors that may have contributed to the high risk associated with older age include social isolation, limited access to care, poor living conditions, and lack of availability of information related to heat-associated risks and their prevention.¹ This crisis raised questions about public health alerts and surveillance.

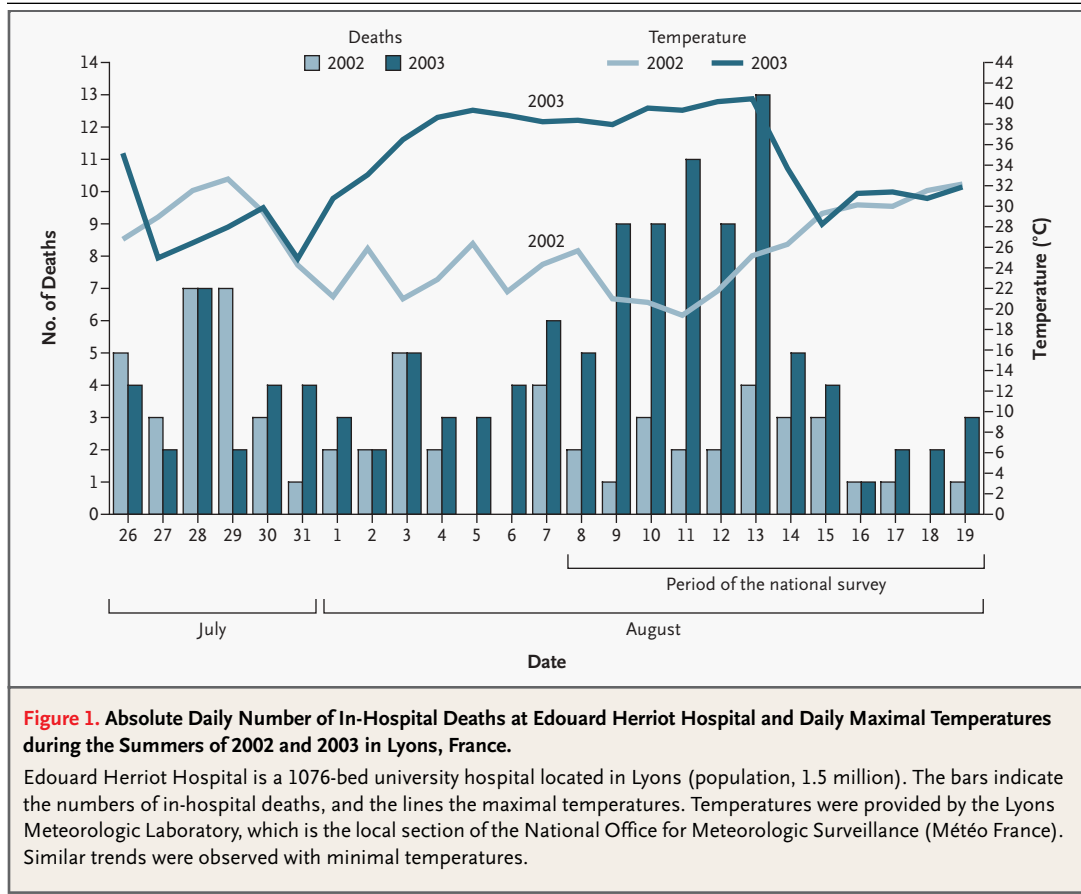
Heat-related mortality may become an increasing concern if global temperatures rise as expected.^{4,5} Reducing such mortality will depend on social, economic, environmental, cultural, and health-related factors.

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1. Semenza JC, Rubin CH, Falter KH, et al. Heat-related death during the July 1995 heat wave in Chicago. *N Engl J Med* 1996;335:84-90.
2. Pattenden S, Nikiforov B, Armstrong BG. Mortality and temperature in Sofia and London. *J Epidemiol Community Health* 2003;57:628-33.

3. Nakai S, Itoh T, Morimoto T. Deaths from heat-stroke in Japan: 1968-1994. *Int J Biometeorol* 1999;43:124-7.
4. O'Neill MS, Zanobetti A, Schwartz J. Modifiers of the temperature and mortality association in seven US cities. *Am J Epidemiol* 2003;157:1074-82.
5. McGeehin MA, Mirabelli M. The potential impact of climate variability and change on temperature-related morbidity and mortality in the United States. *Environ Health Perspect* 2001;109:Suppl 2:185-9.

Treatment of HCV-Related Mantle-Cell Lymphoma with Ribavirin and Pegylated Interferon Alfa

TO THE EDITOR: We expand on the data presented by Hermine et al., who demonstrated the antitumor efficacy of interferon alfa in hepatitis C virus (HCV)-infected patients with marginal-zone lymphoma.¹ We report the details of anti-HCV therapy in the patient from whom we established a B lymphoma cell line that is persistently infected with HCV.² In culture, the line continuously produces

HCV, which can infect primary human hepatocytes, peripheral-blood mononuclear cells, and Raji cells.

In 1995, this patient, a 66-year-old man, was found to have cryoglobulinemia, with elevated levels of rheumatoid factor and creatinine. Antibody to HCV was present; the levels of liver enzymes were normal. A computed tomographic (CT) scan revealed splenomegaly. Bone marrow biopsy revealed