

Drs. Rush and Wright report being employees of BTG International, the company developing the proprietary microfoam Varisolve under an IND application. No other potential conflict of interest relevant to this letter was reported.

1. Ceulen RPM, Sommer A, Vernooij K. Microembolism during foam sclerotherapy of varicose veins. *N Engl J Med* 2008;358:1525-6.
2. Regan JD, Gibson KD, Ferris B, et al. Safety of proprietary sclerosant microfoam for saphenous incompetence in patients with R-to-L shunt: interim report. *J Vasc Interv Radiol* 2008;19: Suppl:S35. abstract.

THE AUTHORS REPLY: Rush and Wright confirm our report on intracardiac gas emboli in both the right and left side of the heart during foam sclerotherapy in patients with patent foramen ovale. However, we describe neurologic signs in two patients after foam sclerotherapy, whereas Rush and Wright state that none of the patients with cerebral foam emboli had neurologic symptoms or cerebral lesions on MRI.

Foam can be produced with a variety of agitation techniques that result in differences in bubble size and rate of reabsorption.¹ We applied the double syringe technique, which led to larger bubbles than Rush and Wright's specifically engineered Varisolve technique to dispense foam hav-

ing a highly controlled bubble-size distribution. Moreover, for polidocanol-foam preparation, Rush and Wright used a very-low-nitrogen gas mixture, whereas we used room air, which is associated with increases in bubble number and size.² Therefore, we believe that the results of the two studies are difficult to compare.

Although we still believe that foam sclerotherapy is a safe procedure and routine screening for patent foramen ovale before foam sclerotherapy is not recommended, we also believe that further research regarding foam characteristics and consequences of foam emboli is necessary.

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1. Eckmann DM, Kobayashi S, Li M. Microvascular embolization following polidocanol microfoam sclerosant administration. *Dermatol Surg* 2005;31:636-43.
2. Regan JD, Gibson KD, Ferris B, et al. Safety of proprietary sclerosant microfoam for saphenous incompetence in patients with R-to-L shunt: interim report. *J Vasc Interv Radiol* 2008;19: Suppl:S35. abstract.

Retraction: Gong Z et al. Injuries after a Typhoon in China. *N Engl J Med* 2007;356:196-7.

TO THE EDITOR: I request that our letter to the editor, "Injuries after a Typhoon in China,"¹ be retracted because much of it was previously published in Chinese journals.^{2,3}

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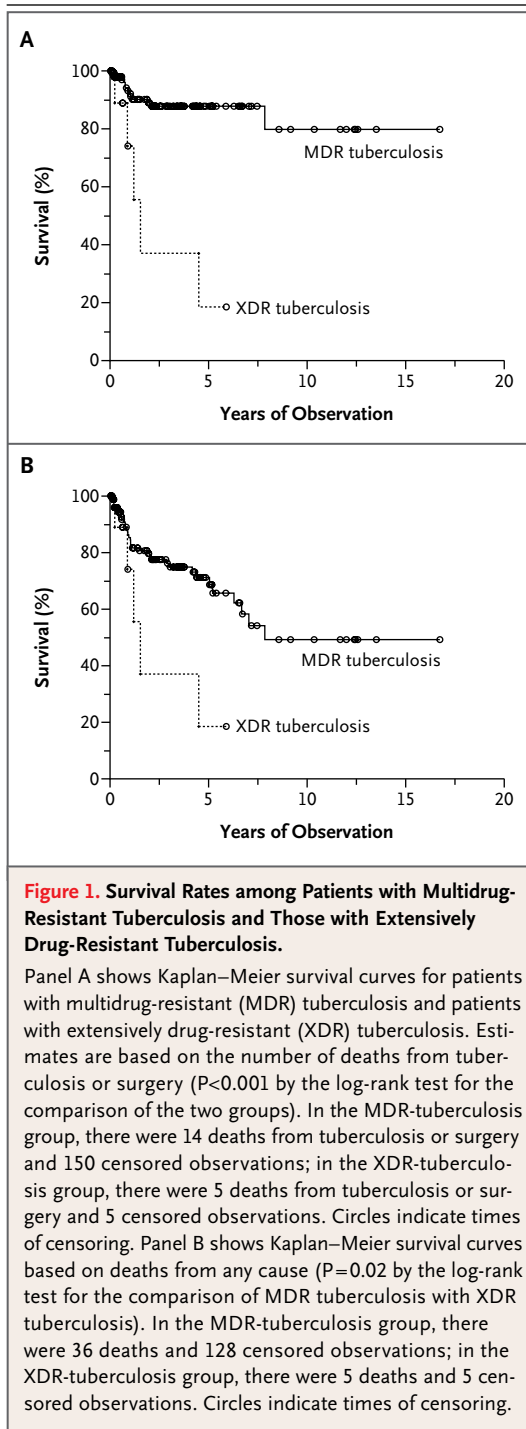
1. Gong Z, Chai C, Tu C, Lin J, Gao Y, Qui Y. Injuries after a typhoon in China. *N Engl J Med* 2007;356:196-7.
2. Gong Z, Chai C, Tu C, et al. Epidemiologic study of the present status of injury to the population caused by typhoon Yunna. *Natl Med J China* 2005;85:3007-9. (In Chinese.)
3. Gong Z, Chai C, Tu C, et al. A field epidemiological study on the risk factors of injury caused by typhoon. *Chin J Epidemiol* 2006;27:773-6. (In Chinese.)

Treatment Outcomes in Extensively Resistant Tuberculosis

TO THE EDITOR: Extensively drug-resistant tuberculosis, which is defined as tuberculosis that is resistant to rifampin, isoniazid, a fluoroquinolone, and a second-line injectable agent, poses a major challenge for global health.¹⁻⁴ There are few published data from studies comparing treat-

ment outcomes for patients with extensively drug-resistant tuberculosis with the outcomes for patients with multidrug-resistant tuberculosis, which is defined as tuberculosis that is resistant to at least isoniazid and rifampin.

Among a series of 205 consecutive patients



who were referred to our specialty medical center for respiratory diseases and treated between 1984 and 1998 for multidrug-resistant tuberculosis, the overall long-term success rate was 75% and the rate of death from tuberculosis was 12%.⁵ We retrospectively analyzed these 205 cases of multi-

drug-resistant tuberculosis⁵ to determine what percentage met the definition of extensively drug-resistant tuberculosis. Using logistic-regression and survival analysis, we then compared the treatment outcomes — defined previously⁵ — in the subgroup of patients with disease that met the definition of extensively drug-resistant tuberculosis with the outcomes in the subgroup with multidrug-resistant tuberculosis that did not meet this definition. This retrospective study was approved by the institutional review board of our center.

In the overall cohort of 205 patients with multidrug-resistant tuberculosis, 174 patients underwent sufficient drug-susceptibility testing to definitively determine whether their disease met the definition of extensively drug-resistant tuberculosis. Of these 174 patients, 10 (6%) were classified as having extensively drug-resistant tuberculosis. A patient's rate of drug resistance was calculated by dividing the number of drugs to which the patient's disease was resistant by the number of drugs tested. The median rate of drug resistance was 45% among patients with multidrug-resistant tuberculosis and 68% among patients with extensively drug-resistant tuberculosis ($P < 0.001$ for the difference by the Wilcoxon rank-sum test). Age, sex, race or ethnic group, the number of patients treated with a fluoroquinolone, the length of time from the diagnosis of tuberculosis to the first visit to our center, the number of patients who underwent lung resection, and the number of drugs used previously did not differ significantly between the two groups ($P \geq 0.19$ for all comparisons, with the use of the Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables).

Logistic-regression analysis yielded odds ratios for treatment success in the group of patients who had multidrug-resistant tuberculosis, as compared with those who had extensively drug-resistant tuberculosis, of 23.4 (95% confidence interval [CI], 4.6 to 188.7) for the initial outcome ($P < 0.001$) and 21.1 (95% CI, 4.2 to 106.8) for the long-term outcome ($P < 0.001$); the length of time from the diagnosis of tuberculosis to the first visit to our center was used as a covariate. In proportional-hazards survival models adjusted for age, the hazard ratio for death from tuberculosis or surgery in the group with extensively drug-resistant tuberculosis, as compared with the group with multidrug-resistant tuberculosis, was

7.9 (95% CI, 2.7 to 23.1; $P < 0.001$), and the hazard ratio for death from any cause was 2.5 (95% CI, 0.9 to 6.5; $P = 0.07$). Estimates were obtained from logistic-regression and survival models adjusted for an expanded set of covariates (surgery, the use or nonuse of fluoroquinolone, the number of drugs used previously, the rate of drug resistance, age, the length of time from the diagnosis of tuberculosis to the first visit to our center, the use or nonuse of a fluoroquinolone according to age, and the use or nonuse of a fluoroquinolone according to the rate of drug resistance). These estimates still showed better outcomes in the group with multidrug-resistant tuberculosis than in the group with extensively drug-resistant tuberculosis. Odds ratios for short-term and long-term treatment success and the hazard ratio for death from tuberculosis or surgery remained significant ($P < 0.05$), with a trend toward significance ($P = 0.15$) for the hazard ratio for death from any cause.

Figure 1 shows Kaplan–Meier estimates of survival based on the number of deaths from tuberculosis or surgery (Panel A) and the number of deaths from any cause (Panel B) among the patients with multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis. The rates of death from tuberculosis or surgery and from any cause were significantly higher among patients with extensively drug-resistant tuberculo-

sis than among patients with multidrug-resistant tuberculosis.

Despite aggressive treatment at our referral center, extensively drug-resistant tuberculosis, as compared with multidrug-resistant tuberculosis, was associated with a significantly poorer initial treatment response and long-term outcome and a significantly lower survival rate. These data underscore the critical importance of optimal management of cases of multidrug-resistant tuberculosis, lest they develop into extensively drug-resistant tuberculosis.

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1. Raviglione MC, Smith IM. XDR tuberculosis — implications for global public health. *N Engl J Med* 2007;356:656-9.
 2. Emergence of *Mycobacterium tuberculosis* with extensive resistance to second-line drugs — worldwide, 2000–2004. *MMWR Morb Mortal Wkly Rep* 2006;55:301-5.
 3. Extensively drug-resistant tuberculosis (XDR-TB): recommendations for prevention and control. *Wkly Epidemiol Rec* 2006;81:430-2.
 4. Gandhi NR, Moll A, Sturm AW, et al. Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. *Lancet* 2006;368:1575-80.
 5. Chan ED, Laurel V, Strand MJ, et al. Treatment and outcome analysis of 205 patients with multidrug-resistant tuberculosis. *Am J Respir Crit Care Med* 2004;169:1103-9.
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