Ebola and Quarantine


The governors of a number of states, including New York and New Jersey, recently imposed 21-day quarantines on health care workers returning to the United States from regions of the world where they may have cared for patients with Ebola virus disease. We understand their motivation for this policy — to protect the citizens of their states from contracting this often-fatal illness. This approach, however, is not scientifically based, is unfair and unwise, and will impede essential efforts to stop these awful outbreaks of Ebola disease at their source, which is the only satisfactory goal. The governors’ action is like driving a carpet tack with a sledgehammer: it gets the job done but overall is more destructive than beneficial.

Health care professionals treating patients with this illness have learned that transmission arises from contact with bodily fluids of a person who is symptomatic — that is, has a fever, vomiting, diarrhea, and malaise. We have very strong reason to believe that transmission occurs when the viral load in bodily fluids is high, on the order of millions of virions per microliter. This recognition has led to the dictum that an asymptomatic person is not contagious; field experience in West Africa has shown that conclusion to be valid. Therefore, an asymptomatic health care worker returning from treating patients with Ebola, even if he or she were infected, would not be contagious. Furthermore, we now know that fever precedes the contagious stage, allowing workers who are unknowingly infected to identify themselves before they become a threat to their community. This understanding is based on more than clinical observation: the sensitive blood polymerase-chain-reaction (PCR) test for Ebola is often negative on the day when fever or other symptoms begin and only becomes reliably positive 2 to 3 days after symptom onset. This point is supported by the fact that of the nurses caring for Thomas Eric Duncan, the man who died from Ebola virus disease in Texas in October, only those who cared for him at the end of his life, when the number of virions he was shedding was likely to be very high, became infected. Notably, Duncan’s family members who were living in the same household for days as he was at the start of his illness did not become infected.

A cynic would say that all these “facts” are derived from observation and that it pays to be 100% safe and to isolate anyone with a remote chance of carrying the virus. What harm can that approach do besides inconveniencing a few health care workers? We strongly disagree. Hundreds of years of experience show that to stop an epidemic of this type requires controlling it at its source. Médecins sans Frontières, the World Health Organization, the U.S. Agency for International Development (USAID), and many other organizations say we need tens of thousands of additional volunteers to control the epidemic. We are far short of that goal, so the need for workers on the ground is great. These responsible, skilled health care workers who are risking their lives to help others are also helping by stemming the epidemic at its source. If we add barriers making it harder for volunteers to return to their community, we are hurting ourselves.

In the end, the calculus is simple, and we think the governors have it wrong. The health care
workers returning from West Africa have been helping others and helping to end the epidemic that has killed thousands of people and scared millions. At this point the public does need assurances that returning workers will have their temperatures and health status monitored according to a set, documented protocol. In the unlikely event that they become febrile, they can follow the example of Craig Spencer, the physician from New York who alerted public health officials of his fever. As we continue to learn more about this virus, its transmission, and associated illness, we must continue to revisit our approach to its control and treatment. We should be guided by the science and not the tremendous fear that this virus evokes.

We should be honoring, not quarantining, health care workers who put their lives at risk not only to save people suffering from Ebola virus disease in West Africa but also to help achieve source control, bringing the world closer to stopping the spread of this killer epidemic.

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**ROS1 — Targeting the One Percent in Lung Cancer**

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Lung cancer is the leading cause of cancer-related death worldwide. For certain patients with non–small-cell lung cancer (NSCLC), molecularly targeted therapies have transformed treatment and improved outcomes. In patients with NSCLC with *EGFR* mutations or *ALK* rearrangements, targeted therapies represent the standard of care, with superior efficacy and improved tolerability, as compared with cytotoxic chemotherapy.1,2 These two genetic alterations are relatively common and are found in about 15% and 5% of patients with NSCLC, respectively. Extensive profiling efforts have identified molecular drivers that are found in smaller subsets of NSCLC, often in just 1 or 2% of patients. Although the incidence of these alterations is low, such targeted therapies can have a major effect, owing to the high prevalence of lung cancer and the potential for dramatic improvements in outcome.

Approximately 1 to 2% of patients with NSCLC have tumors with genetic rearrangements involving the gene encoding ROS1 proto-oncogene receptor tyrosine kinase (ROS1).3,4 Little is known about the role of nonmutant ROS1, which shares structural homology with the insulin receptor family as well as anaplastic lymphoma kinase (ALK). ROS1 is a receptor tyrosine kinase with no known ligands. Chromosomal rearrangements leading to fusion of ROS1 with a number of different partners create a constitutively active kinase that activates the MAP kinase, STAT3, and phosphoinositide 3-kinase (PI3K) pathways, among others, which drive cellular transformation.5 These rearrangements have been described in a variety of tumors in addition to lung cancer, including glioblastomas, cholangiocarcinomas, and gastric cancers. In NSCLC, ROS1 rearrangements are more likely to be found in younger patients, those with adenocarcinoma, and those without a history of tobacco use. In retrospective series, patients with these rearrangements have outcomes similar to those in other patients with NSCLC.3

In this issue of the *Journal*, Shaw and colleagues6 summarize results from an expansion cohort of a phase 1 trial studying crizotinib in patients with NSCLC with ROS1 rearrangements. Crizotinib is an orally administered, small-molecule tyrosine kinase inhibitor with activity against ALK, ROS1, and MET. It is highly effective and has a generally acceptable side-effect profile in patients with ALK-rearranged NSCLC.2 In this study, 50 patients with ROS1-positive NSCLC were treated with crizotinib at a dose of 250 mg twice daily, administered orally. For 98% of patients, ROS1 positivity was determined by break-apart fluorescence in situ hybridization (FISH). Most of the patients (84%) had received previous treatment.

Crizotinib was highly active for these patients, with an overall response rate of 72%.6 In comparison, response rates to cytotoxic chemotherapy in patients with previously treated NSCLC are generally 10% or less.7 Responses to