

to be high in patients with small-cell lung cancer owing to the strong association between the disease and smoking.<sup>1,2</sup> Unfortunately, it is challenging to acquire adequate tissue for extensive molecular testing in patients with small-cell lung cancer, and delaying therapy to repeat biopsies is often not possible. This prompted analysis of alternative biomarkers such as blood-based tumor mutational burden. We hope the role of blood-based tumor mutational burden will further be informed by ongoing trials, such as B-F1RST (ClinicalTrials.gov number, NCT02848651), and other studies.

In reply to Diker: to date, studies evaluating the use of pembrolizumab and nivolumab as maintenance therapies in patients with extensive-stage small-cell lung cancer have failed to show improvements in survival.<sup>3,4</sup> Furthermore, the patient population in maintenance trials is inherently different from those receiving first-line treatment, since only patients with a response or stable disease and adequate performance status and organ function would be eligible. The positive findings from the IMpower133 trial suggest that combining checkpoint inhibitors with cytotoxic chemotherapy in the induction phase and continuing the checkpoint inhibitor into the maintenance phase of treatment may be beneficial.

However, the IMpower133 trial was not designed to evaluate atezolizumab induction separately from atezolizumab maintenance therapy. Further data are therefore needed to understand the role of induction versus maintenance immunotherapy in extensive-stage small-cell lung cancer.

Leora Horn, M.D.

Vanderbilt University Medical Center  
Nashville, TN  
leora.horn@vumc.org

Stephen V. Liu, M.D.

Georgetown University  
Washington, DC

Since publication of their article, the authors report no further potential conflict of interest.

1. Carter BW, Glisson BS, Truong MT, Erasmus JJ. Small cell lung carcinoma: staging, imaging, and treatment considerations. *Radiographics* 2014;34:1707-21.
2. Alexandrov LB, Nik-Zainal S, Wedge DC, et al. Signatures of mutational processes in human cancer. *Nature* 2013;500:415-21.
3. Gadgeel SM, Pennell NA, Fidler MJ, et al. Phase II study of maintenance pembrolizumab in patients with extensive-stage small cell lung cancer (SCLC). *J Thorac Oncol* 2018;13:1393-9.
4. Bristol-Myers Squibb announces CheckMate -451 study did not meet primary endpoint of overall survival with Opdivo plus Yervoy vs. placebo as a maintenance therapy in patients with extensive-stage small cell lung cancer after completion of first-line platinum-based chemotherapy. Press release of Bristol-Myers Squibb, November 26, 2018 (<https://news.bms.com/press-release/corporatefinancial-news/bristol-myers-squibb-announces-checkmate-451-study-did-not-mee>).

DOI: 10.1056/NEJMc1900123

## *Candida auris* in an Intensive Care Setting

**TO THE EDITOR:** Eyre et al. (Oct. 4 issue)<sup>1</sup> report finding that reusable skin-surface axillary temperature probes were the source of a *Candida auris* outbreak in a U.K. intensive care unit. Yeasts persisted on the equipment despite cleaning with wipes containing quaternary ammonium compounds, a procedure that deviated from the manufacturer's instructions. New cases of *C. auris* infection were reduced only after removal of the temperature probes from the wards.

Health care–associated infections from reusable medical devices (including thermometers) are a well-known threat to patient safety, with — in this case — history repeating itself. Another report from the United Kingdom in which thermometers were cited as the potential source of cross-infections among patients was published in 1947,<sup>2</sup> and innumerable reports have appeared

since. Clearly, health care institutions have not learned lessons from the past: manufacturers' instructions are marginalized, and the danger of thermometers is still ignored.

Reports of outbreaks borne by well-known routes continue to be of interest — perhaps especially when caused by an emerging multi-drug-resistant pathogen — but they should serve as a reminder to those of us who provide health care to finally learn from our past and implement needed changes in infection control.

Jacques F. Meis, M.D., Ph.D.

Andreas Voss, M.D., Ph.D.

Radboud University Medical Center  
Nijmegen, the Netherlands  
andreas.voss@radboudumc.nl

No potential conflict of interest relevant to this letter was reported.

1. Eyre DW, Sheppard AE, Madder H, et al. A *Candida auris* outbreak and its control in an intensive care setting. *N Engl J Med* 2018;379:1322-31.
2. Green JB, Penfold JB. Clinical thermometers as a possible source of cross-infection in hospital. *Lancet* 1947;2:89-90.  
DOI: 10.1056/NEJMc1900112

**THE AUTHORS REPLY:** We agree with the need to continue to learn how to implement the best possible infection control for our patients, and the *C. auris* outbreak we described serves as a timely reminder. Infection control needs to minimize risk while being operationally practicable, acceptable to patients, and consistent with the constraints of finite resources. This balance must dynamically adjust as new pathogens emerge. For example, in our situation, the manufacturer's instructions for cleaning and disinfection of the temperature probes made no claim as to their efficacy for infection control.<sup>1</sup> We therefore adopted an alternative unified approach to the cleaning of all noninvasive medical devices, using prepared wipes containing quaternary ammonium compounds. Use of these wipes is widely accepted practice and supported by manufacturer's data on their activity against health care-associated pathogens.<sup>2</sup> However, the emergence of a pathogen with limited susceptibility to quater-

nary ammonium compounds<sup>3</sup> and persistence on environmental surfaces<sup>4</sup> has clearly changed the balance of risk. We therefore agree that there is now a need to act by implementing changes in infection control and renewing vigilance regarding the use of reusable equipment.

David W. Eyre, D.Phil.

University of Oxford  
Oxford, United Kingdom  
david.eyre@ndm.ox.ac.uk

Lisa Butcher, M.Sc.  
Katie J.M. Jeffery, Ph.D.

Oxford University Hospitals NHS Foundation Trust  
Oxford, United Kingdom

Since publication of their article, the authors report no further potential conflict of interest.

1. 21078A skin probe: instructions for use. Amsterdam: Philips Electronics, 2009.
2. Clinell multi-purpose universal wipes. Watford, United Kingdom: GAMA Healthcare, 2015 (<http://clinell.com/product/universal-range/#data>).
3. Cadnum JL, Shaikh AA, Piedrahita CT, et al. Effectiveness of disinfectants against *Candida auris* and other *Candida* species. *Infect Control Hosp Epidemiol* 2017;38:1240-3.
4. Welsh RM, Bentz ML, Shams A, et al. Survival, persistence, and isolation of the emerging multidrug-resistant pathogenic yeast *Candida auris* on a plastic health care surface. *J Clin Microbiol* 2017;55:2996-3005.

DOI: 10.1056/NEJMc1900112

## The Role of Deferiprone in Iron Chelation

**TO THE EDITOR:** In their review article, Hider and Hoffbrand (Nov. 29 issue)<sup>1</sup> focus on iron chelation in patients with neurodegenerative diseases. However, we were disappointed that there was no mention of classic superficial siderosis of the central nervous system, one of the few progressive neurologic conditions for which iron chelation with deferiprone is currently used as a treatment.<sup>2,3</sup>

Classic superficial siderosis is characterized by hemosiderin deposits (typically in the superior cerebellar vermis, brain stem, and spinal cord)<sup>2</sup> that are easily identified on blood-sensitive magnetic resonance imaging (MRI) sequences. This condition is usually associated with the classic clinical triad of sensorineural hearing loss, ataxia, and myelopathy. The usual underlying cause of classic superficial siderosis is chronic low-volume subarachnoid hemorrhage,<sup>4</sup> which is often associated with a traumatic or postsurgical dural de-

fect. Although radiologic or surgical treatment of the source of bleeding is preferred, in patients in whom no such "leak" can be identified or repaired (or in those who cannot receive invasive treatment), iron chelation is an alternative or adjunctive option.<sup>2</sup>

Initial observational data on the use of deferiprone in patients with superficial siderosis are promising.<sup>3</sup> However, data from randomized, controlled trials on efficacy and toxic effects (including agranulocytosis)<sup>5</sup> are lacking.

Gargi Banerjee, M.R.C.P.  
Yezen Sammariaee, M.B., B.S.  
David J. Werring, Ph.D., F.R.C.P.

University College London Queen Square Institute of Neurology  
London, United Kingdom  
d.werring@ucl.ac.uk

No potential conflict of interest relevant to this letter was reported.