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Financial/nonfinancial disclosures: The authors have reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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Response

To the Editor:

I thank Dr Farkas and colleagues for their interest in our study on the potential risks of developing Pneumocystis pneumonia (PCP) in patients with compromised immune systems receiving rituximab. The letter raises the important question about whether the three patients reported in the case series might actually represent colonization rather than PCP. This question arose because the cases were detected by polymerase chain reaction (PCR) assay. We believe that these cases represent true PCP rather than colonization; thus, further clarification is needed.

Many PCR assays reported in the literature amplify mitochondrial DNA sequences. Hence, they amplify multicopy Pneumocystis target genes, significantly heightening detection sensitivity. In addition, these assays often rely on nested PCR approaches where the initial amplification products are subsequently reamplified, yielding even greater sensitivity. Indeed, such approaches may be overly sensitive for many routine clinical applications. Accordingly, previously reported PCR assay approaches are known to detect Pneumocystis colonization in addition to invasive infections. However, the Pneumocystis PCR assay used in our clinical microbiology laboratory has unique features that circumvent many of these issues. To address the issues of colonization, we use a diagnostic Pneumocystis PCR assay that uses a single-copy target gene from Pneumocystis jirovecii, namely pjcd2. We also perform quantitative amplification with real-time PCR and do not reamplify the reaction products with nested PCR. With this PCR assay, we have observed an increase (approximately 7%) in total diagnostic sensitivity over smeared stains alone. In addition, in now > 200 consecutive cases without clinical evidence of infection, we have not detected a PCR signal. Hence, the assay used in this study was specifically designed to detect PCP rather than colonization. On this basis, our laboratory now routinely uses this PCR assay rather than microscopic examination for the diagnosis of Pneumocystis infection. Moreover, it must be noted that the patients in the current report had active lung infiltration as well as signs and symptoms of infection. In each patient, there was no evidence of any other significant alternative organism, despite routine comprehensive culture, antigen detection, and molecular diagnostic assays performed to rigorously detect typical and atypical bacteria, viruses, and other fungi. Thus, in all three patients, the clinical evidence pointed to active PCP rather than to colonization.

Andrew H. Limper, MD, FCCP
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Recovery of Consciousness After Head Injury

To the Editor:

Luce1 is to be commended for his excellent review on chronic disorders of consciousness following coma that recently published in CHEST (October 2013). Nevertheless, we wish to point out that, in our opinion, the author is inaccurate in stating that “coma following TBI [traumatic brain injury] usually is manifested pathologically by diffuse axonal injury; which also is called traumatic injury, involving the cerebral cortices and brain stem.”

The mechanisms involved in TBI and coma are actually complex and often multifactorial. Focal lesions (extradural and subdural hematomas, intraparenchymal hematomas and contusions), diffuse lesions (swelling, diffuse axonal injury [DAI], posttraumatic subarachnoid hemorrhage), and biochemical derangements can act as independent or associated causes of coma after TBI. The variety

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Financial/nonfinancial disclosures: The author has reported to CHEST the following conflicts. Dr Limper is coinventor of the pjcd2 diagnostic PCR assay discussed in this report and holds a patent on this method.

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Psyciatric Morbidity in Patients With Lung Cancer

To the Editor:

The article by Urban et al in CHEST (October 2013) made for an interesting read. We appreciate the authors’ earnest attempt to identify the subpopulation of patients with lung cancer at risk for committing suicide following diagnosis. The authors documented the highest standardized mortality ratios (SMRs) in male patients, older patients, patients with a higher-grade tumor and metastatic disease, and patients who did not receive, or refused, treatment. Despite the higher SMR among patients with metastatic disease, the finding that >50% of suicides occurred in those with locoregional and potentially curable disease and that a majority of suicides occurred within 3 months of diagnosis raises a great degree of concern.

It is possible that a significant proportion of the subset of patients with lung cancer who committed suicide despite locoregional or potentially curable illness also suffered from comorbid (preexisting) depressive disorder or other psychiatric illnesses. Various studies have reported the presence of psychiatric illness in the majority of suicide completers in the general population, ranging from 81% to 100%. A few studies have documented depressive disorder as a risk factor for the development of lung cancer. For example, Chen et al found depressive disorder in 4.91% of subjects at risk for lung cancer. Hence, it is highly likely that not adjusting for psychiatric disorders, particularly depressive disorder, as a confounding variable in this population would have resulted in an inaccurate estimation of SMR.

It would have been ideal had the authors carried out psychologic autopsy in addition to their study of registry data. Although a cumbersome procedure, psychologic autopsy is a valuable research tool for completed suicides that retrospectively collects all available information on the deceased patient through structured interviews of family members, relatives, friends, and treating health-care personnel. In addition, information is collected from available health-care or psychiatric records, other documents, and forensic examination. Thus, a psychologic autopsy collaterally synthesizes information from various sources, providing clues regarding possible psychiatric morbidity prior to suicide apart from a systematic

**REFERENCES**


**Response**

To the Editor:

I thank Dr Gemma and colleagues for more fully explaining the pathologic manifestations of traumatic brain injury in their letter. I was unable to do so in my review of chronic disorders of consciousness following coma1 because of space limitations.

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**Financial/nonfinancial disclosures:** The author has reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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DOI: 10.1378/chest.13-2710