

ens existing pulmonary hypertension. We recommend that all patients with PPH should be screened for possible coexisting hypothyroidism.

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**In Reply:** Drs Kashyap and Kashyap are correct in highlighting the association between PPH and thyroid disease and in recommending that all patients with PPH be screened for hypothyroidism.<sup>1</sup> Thyroid disease, either hypothyroidism or indeed hyperthyroidism,<sup>2</sup> can occur at any stage in the course of PPH and should be considered whenever there is an abrupt change in clinical status, such as new tachycardia, unexplained weight loss, worsening right heart failure, or new pericardial effusion. While autoimmune features are occasionally seen in PPH, the majority of patients do not have Raynaud phenomenon or the presence of autoantibodies. The recent discovery that heterozygous mutations within the bone morphogenetic protein type II receptor gene of the transforming growth factor  $\beta$  cell-signaling superfamily have been identified in familial and sporadic cases of PPH argues against autoimmunity as the cause of PPH.<sup>3,4</sup> However, as understanding of the pathobiology of PPH advances rapidly, a clearer explanation for the observed association between PPH and thyroid disease will no doubt become apparent.

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## Causes of Traumatic Death During Pregnancy

**To the Editor:** In their article about pregnancy-associated mortality, Drs Horon and Cheng<sup>1</sup> emphasized the need to move beyond traditional definitions of maternal mortality. It is also important to move beyond the perception that homicide is the

only major contributor to pregnancy-associated injury mortality. Although Horon and Cheng indicated that some pregnancies in their study were undetected, they did not address the limitation of the sample's representativeness. Another issue is the difficulty detecting all pregnancies in motor vehicle traffic (MVT) deaths.

The policy of the Maryland medical examiner's office is to perform an autopsy for all cases of homicide. For MVT-related deaths, the usual policy is to perform an autopsy on drivers who die after a brief hospitalization, but passengers are generally not examined unless they are the only fatality (John Smialek, MD, chief medical examiner, state of Maryland, oral communication, March 23, 2001). The Federal Fatal Accident Reporting System reported 86 deaths among Maryland women aged 15 to 44 years in 1998. Among these, 49% were listed as drivers. Because medical examiner reports were a substantial source of pregnancy-associated homicide deaths in the study by Horon and Cheng and comprised 100% of the homicides during pregnancy, there is a selection bias that undercounts MVT deaths. My discussions with Dr Horon suggest that about one third of motor vehicle occupants who were killed did not undergo autopsy, and so some early pregnancy MVT cases may have been missed.

National representativeness is a concern because Maryland has a high proportion of homicide vs MVT mortality compared with the proportion for the entire United States. Between 1993 and 1998, among Maryland women aged 15 to 44 years, there were 499 homicides and 605 MVT deaths (0.82 ratio of homicide to MVT). In comparison, in the entire United States, there were 19306 homicides and 41474 MVT deaths (0.47 ratio).<sup>2</sup>

One other way in which MVT deaths during pregnancy were minimized was through selective referencing. Citations in the article reported homicide as the leading cause of pregnancy-associated death. However, these studies were derived from highly urbanized areas (ie, New York and Chicago). Among studies that have encompassed urban and nonurban areas, the contributions from homicides and MVT deaths during pregnancy have been about equal.<sup>3</sup> Several studies have reported proportional mortality for MVT to be greater.<sup>4,5</sup> An age- and birth-adjusted calculation using 1996 US mortality data (assuming no pregnancy influence on rates) results in estimates of 155 (mostly firearm-related) homicides and 368 MVT deaths to pregnant women. If homicide rates moderately increased and/or MVT mortality rates moderately decreased during pregnancy in women, this would be consistent with the relatively similar rates observed in broader population-based studies.

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1. Horon I, Cheng D. Enhanced surveillance for pregnancy-associated mortality—Maryland, 1993-1998. *JAMA*. 2001;285:1455-1459.
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**In Reply:** Dr. Weiss criticizes us for minimizing the importance of MVT as a cause of pregnancy-associated mortality by failing to detect a large proportion of MVT deaths in our case identification as well as for “selective referencing.” Both criticisms lack merit.

As we point out in our article, we may not have identified some deaths that occurred during early pregnancy if an autopsy was not performed. However, Maryland law mandates that the medical examiner investigates all deaths that occur by violence, suicide, injury, unexpectedly, or in any suspicious or unusual manner, all MVT deaths are investigated by the medical examiner. Although an autopsy is not performed in all cases of MVT death, the medical examiner notes and police records are often available for review even if an autopsy was not performed. If pregnancy was noted in such records in our review of medical examiner data, the death was included in our study.

In the years 1993-1998, an autopsy was performed in 67% of all women between the ages of 15 and 44 years who died from MVT-related causes. This includes 84% of drivers, 73% of pedestrians, and 50% of passengers. Assuming that those who did not undergo autopsy (n=177) had the same likelihood of pregnancy as those who did (16/409), we would have identified 7 additional MVT deaths. Therefore, at most, there would have been a total of 23 pregnancy-associated deaths resulting from MVT, which is less than half the number of homicide deaths we identified.

Weiss also states that we minimized the importance of MVT as a cause of pregnancy-associated mortality through “selective referencing.” We do not, as Weiss claims, provide citations that report homicide as the leading cause of death to the exclusion of articles that refute this point. Other reports have identified homicide as a cause of pregnancy-associated death. However, we are not aware of any previous studies that use multiple data sources to comprehensively identify all pregnancy-associated deaths (both during pregnancy and within a year of delivery or pregnancy termination) from all causes, as we did. Therefore, we believe our study is the first to provide a complete ranking of all pregnancy-associated deaths by cause.

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### Interobserver Agreement About Cervical Cytologic and Histologic Diagnosis

**To the Editor:** In the study reported by Drs Stoler and Schiffman,<sup>1</sup> there was a surprisingly high degree of variability in the interpretation of results of histologic and cytologic cervical speci-

mens. Considering the modest degree of reproducibility in these academic centers, this is surely a cause for humility. There are, however, inherent difficulties with such interpretations. Each cell in a cytologic preparation represents a point in a continuum from normal to neoplastic, but a diagnosis represents a summary of decisions about the significance of many cells at different stages. The reproducibility of a diagnosis of individual cells would be another interesting study of reproducibility.

This study was performed in an idealized setting, with no apparent time constraints on review. This difference from clinical practice may or may not improve the results. The authors speculate that this study “probably underestimate(s) the level of variability between groups of pathologists nationally,” and that “academic pathologists with a research interest in cervical cancer precursor interpretation management” have superior skills than those who read cytologic specimens in commercial laboratories, with “decreasing opportunities” for cytohistologic correlation in “this unfortunate economic reorganization of cytopathology practice.”

However, Stoler and Schiffman may underestimate the functioning of the free market, which demands a balance of quality, service (including turn-around times), and cost. They imply that clinicians who entrust these laboratories with their patient’s biopsy samples have no expectations of reproducibility and correlation with diagnoses.

Atypical cells of uncertain significance (ASCUS) seemed to provide the greatest source of difficulty. The study demonstrated that of 1473 interpretations of ASCUS by clinical centers, only 43% were concurred by quality control (QC) pathologists, who rendered less severe readings for most of the rest of the specimens. It is possible that the purposes of each group differed; the clinical pathologists are attempting to provide guidance, while the QC pathologists, at their leisure, were scrutinizing these cases from a more academic perspective. More valid comparisons would subject both groups to the same time and outcome demands.

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1. Stoler MH, Schiffman M. Interobserver reproducibility of cervical cytologic and histologic interpretation: realistic estimates from the ASCUS-LSIL Triage Study. *JAMA.* 2001;285:1500-1505.

**In Reply:** Dr Mulkey raises 2 concerns about the validity of comparing clinical center to QC diagnoses: (1) that QC diagnoses were rendered “in an idealized setting, with no apparent time restraints on review” which is different from clinical practice and (2) that the QC diagnoses were used for academic and not for patient care purposes. In fact, the workload of both the clinical centers and the QC pathologist in this large trial was extremely demanding and precluded the luxury of leisurely review. Moreover, an important purpose of the QC review was to serve as a safety net and to ensure all involved that the patients could be followed up throughout the trial with-