Merchant et al., by using *ung+* and *ung– Escherichia coli* strains, demonstrated that total nitric oxide exposures in the μmol/L range can lead to C→T mutations by a mechanism probably involving cytosine deamination (8). On the other hand, in *M. smegmatis*, the abrogation of the Ung activity leads not only to increased mutator phenotype but also to growth inhibition by reactive nitrogen intermediates (7). In summary, I speculate that mutations in *ung* that do not completely impair function, but do decrease synthesis of its product, might tolerably increase the spontaneous C→T mutations, including those in the respective positions in the *rpoB* codons 531 and 526. This assumption seems likely because both of the aforementioned particular mutations were described in spontaneous mutants of H37Rv obtained in vitro and had a Darwinian fitness slightly less than or equal to that of the *rpoB* wild-type-susceptible parental strain (9). In contrast, the translesion synthesis-based pathways appear less likely to contribute to emergence of such mutants, although at least one of the translesion synthesis genes (*dinP*) is present in the genome of *M. tuberculosis*. In the *E. coli* in vitro model, a translesion synthesis enzyme (*dinB* encoded DNA polymerase IV) activity clearly promoted more important frameshift mutations (single-base deletions) in two thirds of the spontaneous mutants (10).

From an evolutionary point of view, the multiple *rpoB* mutations in *M. tuberculosis* have been hypothesized to arise as a compensatory mechanism to ameliorate the fitness costs of the original resistance mutation by a secondary mutation (11). The process of adaptation to the fitness costs of chromosomally encoded resistance has been studied in *E. coli* and *Salmonella enterica* serovar Typhi for mutations that affect translation in the *rpsL* and *fusR* genes (11) and for *rpoB* mutations in *E. coli* K12 strain (11). In the last instance, the *rpoB* multiple mutants were selected in vitro in a stepwise fashion, and one double mutant, L511Q+D516G (also described in *M. tuberculosis* strain [3]), exhibited a relative fitness either greater than or equal to either single mutant or the wild type. Reynolds (11) suggested that this allele is favored not merely as a combination of two low-level resistance mutations but also because these mutations together boost resistance and preserve fitness. Whether the same is true for other multiple mutant alleles in *M. tuberculosis rpoB* remains to be seen. Studying the costs of resistance of multiple *rpoB* mutations in a more realistic environment of animal models of TB infection seems promising.

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Human Metapneumovirus and Chronic Obstructive Pulmonary Disease

To the Editor: We read with interest an article, Human Metapneumovirus Detection in Patients with Severe Acute Respiratory Syndrome, in your journal (1). In the report, Chan et al., did not question that SARS-CoV is the etiologic agent of severe acute respiratory syndrome (SARS); however, human metapneumovirus (HMPV) was found in 25 (52%) of 48 probable SARS cases that were investigated, and SARS-CoV was detected in 11 (22.9%) of them. Another recent article reported HMPV in five of six patients in whom SARS was diagnosed in Canada (2); four of the six were coinfected with

SARS-CoV. The prevalence of HMPV infection in SARS patients validates the interest in HMPV's possible role in SARS etiology.

From November 2001 to February 2002, 1 year before the first cases of SARS appeared, we tested the sputum of patients >64 years of age who had experienced exacerbation of chronic obstructive pulmonary disease, for HMPV. Investigations were conducted on 90 episodes in 89 elderly patients, 62 males and 27 females, in which we found no other microorganisms that could have been related to the exacerbation of chronic obstructive pulmonary disease. RNA was extracted from the sputum samples and amplified by reverse transcriptase–polymerase chain reaction (RT-PCR) to detect HMPV as previously described (3). Results of bacterial culture and culture and PCR to detect respiratory syncytial virus and influenza virus types A and B were negative, whereas HMPV was found in the sputum of five (three men and two women) immunocompetent patients, 77–87 years of age. The prevalence of HMPV infection was 5.5%, similar to the percentage obtained by Chan et al., when HMPV RT-PCR was conducted on the respiratory samples. Fever (temperature >38ºC) was not present in any of the five patients infected with HMPV. Two patients were admitted to a hospital. Both patients had bronchial infection and cough with bronchospasm and moderate respiratory insufficiency (oxygen saturation rate: 90.3% and 88%, respectively) for >1 week. Sputum samples from an additional 70 elderly patients with exacerbation of chronic obstructive pulmonary disease with positive detection for influenza virus (n = 50) or respiratory syncytial virus (n = 20) were tested for HMPV infection. None of the samples showed HMPV infection.

Sequence analysis of amplicons from the five samples positive for HMPV infection showed >95% similarity with HMPV sequences found in other parts of the world (4,5). Additional studies should be conducted to confirm that HMPV exacerbates chronic obstructive pulmonary disease. However, by performing an RT-PCR directly on the sample instead of the more efficient RT-PCR after viral culture used by Chan et al., these findings suggest that HMPV is a frequently undetected agent in acute respiratory infection unrelated to SARS. The important questions are whether HMPV and SARS-CoV coinfection would facilitate more severe SARS, or whether HMPV infection would facilitate a more efficient transmission of SARS-CoV.

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Integrons in *Salmonella* Keurmassar, Senegal

To the Editor: Infections caused by *Salmonella* are the primary cause of foodborne diseases; multidrug resistance to *Salmonella enterica* subsp. *enterica* is increasing. The selective pressure created by the widespread use of antimicrobial agents in animals and humans as prophylactic and therapeutic agents may have contributed to the dissemination of resistant bacterial strains. In 2000, the new serovar Keurmassar (35:c:1,2) of *S. enterica*, was described in Senegal (1). Integrons are efficient gene-capture systems by site-specific recombination and are involved in antimicrobial-drug resistance in gram-negative bacteria (2). Three classes of integrons are well characterized and are involved in antimicrobial resistance. Integrons have been found in different nontyphoidal serovars of *S. enterica* and recently in serovar Typhi (3).

We evaluated the contribution of integrons to the antimicrobial drug resistance of eight isolates of *S. enterica* serovar Keurmassar sent to the Senegalese National *Salmonella* and *Shigella* Reference Laboratory at the Pasteur Institute in Dakar from March to May 2000. One strain was isolated from poultry flesh, and seven strains were isolated from human stool or blood samples. Susceptibility testing was performed by disk diffusion method on Mueller-Hinton agar according to the Comité de l'antibiogramme, Société Française de Microbiologie, recommendations. The eight strains expressed an extended-spectrum β-lactamase, which was previously identified as SHV-12 (1). The strains were also resistant to aminoglycosides (amikacin, gentamicin, netilmicin, spectinomycin, streptomycin, and