

azithromycin (1 g) was given for possible chlamydial infection with Reiter's syndrome. PCR for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* from urethral swab was negative, dark field microscopy of the ulcer did not show spirochetes. HIV viral load, *Treponema pallidum* haemagglutination test, and Venereal Disease Research Laboratory test were negative, as was the test for HLA B27.

Although skin lesions were absent, the combination of stomatitis, conjunctivitis, and urethritis was suggestive for Stevens-Johnson syndrome. Incomplete presentation of this syndrome associated with *M pneumoniae* infection has been reported,^{2,3} but exclusively in children. Because of the atypical pneumonia in combination with incomplete Stevens-Johnson syndrome, a PCR was done on oral swab material taken on the day of admission. This showed the presence of *M pneumoniae* DNA. Diagnosis was

confirmed by serology (agglutination IgM/IgG titre 1/20480). The patient recovered completely after additional azithromycin therapy. There was no relapse and currently he is in excellent clinical condition.

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Rocky Mountain spotted fever in the USA: a benign disease or a common diagnostic error?

A recent Review¹ and comment² on Rocky Mountain spotted fever (RMSF), a tickborne infection caused by *Rickettsia rickettsii*, outlined several important aspects of this severe disease; absent, however, was a discussion about the apparent and striking decline of the US case-fatality rate of RMSF during the past 25 years. Since its initial description in the late 19th century, RMSF has been described consistently as a remarkably lethal infection. Indeed, 96 (63%) of 153 patients from Montana diagnosed with RMSF during 1904–13 died from this disease.³ Even with advances in supportive medical care, the aggregate case-fatality rate of RMSF was approximately 23% in the decade preceding the discovery of appropriate antimicrobial therapy for this disease in the late 1940s.⁴ Case-fatality rates that exceed this percentage are still reported from many South American countries, including Argentina, Brazil, and Colombia.⁵ Since 2000, the number of reported cases of RMSF in the USA has increased during all but a single year, with a peak in 2006 (2288 cases; figure). However, in 1997–2002, the overall case-fatality rate was estimated at 1.4% (range 0.7–2.9%).⁶ Furthermore, in the recently published

Summary of notifiable diseases—United States, 2006, a total of 3908 cases of RMSF were notified in 2002–04, including 22 deaths—that is a case-fatality rate of 0.7%.⁷ This is much lower than the case-fatality rates

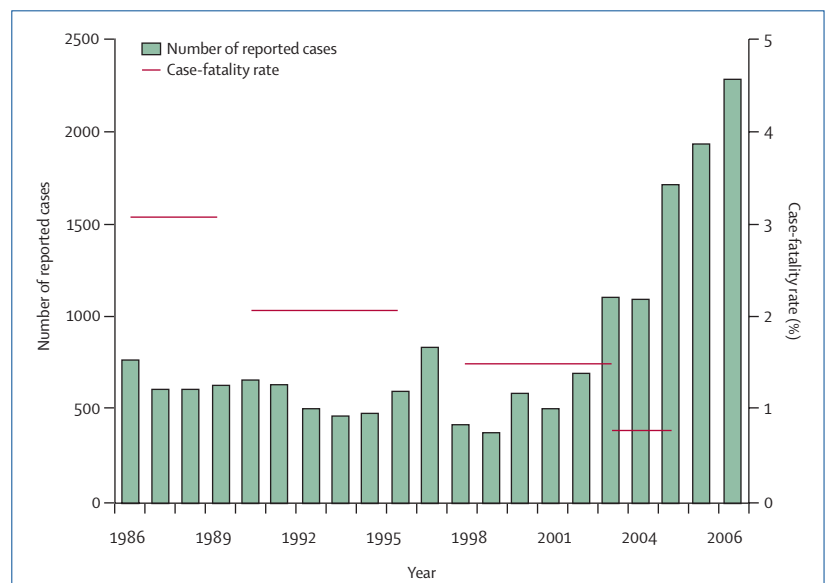


Figure: Reported cases of so-called Rocky Mountain spotted fever and case-fatality rates in the USA
From data in reference 7.

reported for legionellosis (4%), listeriosis (4.8%), or meningococcal disease (9.3%).⁷

This paradoxical finding requires explanation. There are few reasons to believe that the fatal cases are currently more commonly unrecognised than benign cases. One possible explanation is that diagnostic criteria are not specific and that RMSF is confused with other less severe rickettsioses. Most RMSF-diagnosed cases reported to the US Centers for Disease Control and Prevention are based on serological or immunohistochemical tests that do not specifically identify *Rickettsia*.⁸ We found recently that at least a third of cases of "RMSF" that had been serologically confirmed by immunofluorescence antibody tests were likely to be infections caused by *Rickettsia parkeri*, based on western blot analysis.⁹ Other US rickettsial pathogens or potential pathogens with serological cross-reactivity with *Rickettsia* include *Rickettsia massiliae*,¹⁰ *Rickettsia amblyommii*,¹¹ *Rickettsia akari*, and *Rickettsia felis*.¹¹ Moreover, 15% of RMSF cases reported in 2006 occurred during December and January, findings that contradict the typically described spring-summer seasonality of RMSF recognised for more than a century. The same phenomenon, reported for Mediterranean spotted fever during the 1980s, was in fact ultimately determined to be caused by a rickettsiosis that occurred in winter caused by *Rickettsia slovaca*.¹² It is possible that a relatively benign rickettsiosis might be similarly responsible for wintertime cases of "RMSF". It is also possible that imported cases of African tick bite fever in travellers¹³ are incorrectly reported as RMSF.

Another explanation could be that there are variations in virulence in some *Rickettsia* strains. Early descriptions of RMSF during the 19th century remarked that the severity of cases from Idaho (5% case-fatality rate) and Montana (70–80% case-fatality rate) were very different.¹⁴ This variation in potential virulence of different *Rickettsia* strains has since been neglected. A recent study found four main genotypes of *Rickettsia*; however, it remains uncertain if these genotypes are associated with any measurable differences in virulence.¹⁵

The low case-fatality rate of so-called RMSF in recent years in the USA contradicts most of the current reviews and book chapters on this disease. This disparity could be because of a simple repetition of previous chapters without updating. One possible

explanation of the persistence of the claim that RMSF is highly fatal in the USA might be related to the fact that the US reference author is a pathologist whose experience of the disease is based on autopsies of fatal cases.¹⁶

In conclusion, we believe that, like in many other countries around the world, there are several rickettsial diseases circulating in the USA and that the discovery of these additional cases requires further investigation. Because other rickettsial diseases are likely being grouped under the generic name "RMSF", the fatality rate of RMSF in the USA is now very low, contradicting over a century of clinical awareness of this disease. The factors responsible for lower fatality rates, the increase of reported cases, and the increase in winter cases should prompt an active strategy to understand the current distributions of rickettsial diseases in the USA and to assess the true prevalence of *Rickettsia* infections.

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Human papillomavirus vaccines: a complex decision focused on cancer prevention and cost-effectiveness

Sarah Hull and Arthur Caplan¹ discuss choosing between GlaxoSmithKline's Cervarix and Merck's Gardasil for vaccination against human papillomavirus (HPV), but miss the true complexity of public-health decision making.

Modelling indicates that the impact of HPV16/18 vaccination on cervical cancer probably depends on duration of protection.^{2,3} Cervarix (HPV16/18) generates a strong antibody response, potentially indicating longer protection and reduced need for booster vaccination; evidence of cross-protection against HPV45 is also relevant. These findings can only be fully assessed over years, but may outweigh benefits of HPV6/11 (Gardasil) protection.

Global public-health importance clearly rests with HPV16 and HPV18 for cervical and other cancers. HPV6 and HPV11 cause genital warts and juvenile-onset recurrent respiratory papillomatosis (JORRP), but JORRP has a low incidence (1.1 per 100 000 population per year in the USA). Comparisons need to be made with potential interventions in other rare but serious diseases; no health system can deliver everything, and therefore rationing is inevitable. A full discussion of HPV vaccination must consider all the benefits and costs of both vaccines and, if a price difference between Gardasil and Cervarix exists, other affordable health measures. In

the UK, choices might include costly treatments against macular degeneration or other cancers, or extending HPV16/18 vaccination provision internationally. Societal impact of cervical cancer is vast, causing death in women responsible for young children and greater years-of-life-lost in eastern Europe, Latin America, and the Caribbean than tuberculosis, AIDS, and maternal conditions.⁴

Careful appraisal of evidence and health economic analysis produces clear and well-informed debate. Letting a single issue drive an important decision may, through inappropriate use of resources, result in more women experiencing avoidable cervical cancer.

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