In response to an earlier letter, details of the abundance and characteristics of CO_2 clathrate-hydrates under martian conditions are presented to explain why such clathrates could not have been involved in the loss of the Mars Polar Lander mission. Whether the current epidemic of human *Salmonella enteritidis* infections, particularly in the United Kingdom, began in the 1960s or 1980s is debated. And a hypothesis about the origins of this epidemic, "that eradication of [*Salmonella*] *gallinarum*... opened an ecological niche that allowed... *S. enteritidis* strains to be introduced into poultry flocks from their rodent animal reservoir," is discussed, including whether sources other than poultry might be to blame.

Clathrates Are Not the Culprit

A. F. Koster van Groos and S. Guggenheim suggest in their letter that clathrates might have played a role in the loss of the Mars Polar Lander mission (*Science*'s Compass, 11 Feb., p. 973). However, no significant amount of clathrates could exist near the surface of Mars. The average annual surface temperature at the landing site is about 205 kelvin, in comparison with an upper limit of about 151 kelvin for CO_2 clathrate-hydrate stability (*1*) at martian surface pressures [~450 pascal at the landing site elevation of about +2 km (*2*)]. Also, this average temperature will increase with depth. Thus, the only clathrate possible (relevant to the landing) would have to have formed during the prior winter, when surface temperatures are buffered by seasonal CO_2 condensation at 143 kelvin (at these elevations).

CREDIT: PHOTO COURTESY LOCKHEED MARTIN

Had the Mars landing gone as planned... (an artist's rendition).

The atmosphere at south polar latitudes is relatively dry, even for Mars (*3*), and the proportion of H_2O present in the seasonal CO_2 deposit is almost certainly no more than its global annual average in the atmosphere, about 0.0001 by mass (*4*). The seasonal CO_2 accumulation at the landing region is about 1000 kg/m^2 (*5*). Carbon dioxide in a clathrate-hydrate is present in a ratio of 1/6 with the H_2O molecules. This yields an upper limit on clathrate abundance of 0.1 kg/m^2 and no more than about 0.03 kg/m^2 of the trapped-gas release. This amount of volatile material could not have disrupted the landing process.

In addition, the forecast of surface conditions based on Mars Global Surveyor (MGS) and historical observations (*6*) was that the seasonal CO_2 deposit would be gone by 7 November 1999, a month before the landing; this was confirmed by continuing MGS monitoring activities. Once the pure CO_2 deposit was gone, the residue seasonal H_2O frost, clathrate or not, would sublime in less than 30 minutes of natural sunlight.

Hugh H. Kieffer
U.S. Geological Survey, 2255 North Gemini Drive, Flagstaff, AZ 86001, USA. E-mail: hkieffer@usgs.gov

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Salmonella enteritidis Epidemic

A. J. Bäumler, B. M. Hargis, and R. M. Tsolis suggest in their Perspective "Tracing the origins of *Salmonella* outbreaks" (*Science*'s Compass, 7 Jan., p. 50) that the current worldwide epidemic of *S. enteritidis* might have started in the late 1960s rather than in the 1980s. They cite three publications from the Public Health Laboratory Service of England and Wales (*1*); however, they do not provide information about the annual incidence of infections nor data on individual phage types of *S. enteritidis*. This information is vital to an understanding of the epidemic of *S. enteritidis* infection in the United Kingdom.

The current U.K. epidemic of *S. enteritidis* has been caused predominantly by a strain of phage type 4 (PT4). Infections have been associated with poultry and poultry products, particularly the contents of whole-shell eggs. The latter vehicle has provided a new dimension for *S. enteritidis*, and many large outbreaks have been linked to eggs rather than poultry meat (*2*).

From 1961 to 1970 the total number of people infected in the United Kingdom with *S. enteritidis* increased from 151 to 913 per annum. However, the most common phage type isolated was PT8, which was responsible for several substantial turkey-associated outbreaks in the late 1960s. Isolations of PT4 increased only moderately during this period, from 18 in 1961 to 109 in 1970. Although there was a doubling in the incidence of PT4 from 1969 to 1970, many infections were associated with foreign travel. From 1971 to 1980, isolations of *S. enteritidis* ranged from 651 to 879 per annum, with PT8 remaining the most common phage type. In 1983, PT4 became predominant, comprising 46% of 1774 isolations that year. The most dramatic increase was seen in 1987–88, when isolations of *S. enteritidis* increased from 6858 to 15,427, with PT4 comprising 81% of strains isolated (*3, 4*).

If these data are plotted on a logarithmic scale, a steady increase in isolations from the mid-1960s to 1981 is apparent. The epidemic of PT4 most likely commenced in 1982–83. Subsequent epidemiological investigations have indicated that poultry breeding lines infected with PT4 were introduced into the United Kingdom around this time, probably originating in elite flocks in continental Europe. We therefore conclude that the epidemic of *S. enteritidis* PT4 in the United Kingdom started in the early 1980s, and not in the late 1960s.

The largest number of isolations of PT4 was recorded in 1993, when 17,371 infections were identified (*4*). There has been a dramatic decline since 1997, with around 6700 isolations of PT4 identified in 1999 (*5*). The reasons for this decline are multifactoral, including that several codes of practice for the control of salmonellas in chickens have been in operation in the United Kingdom since 1993; there have been many improvements in the poultry industry in infection control and hygiene at breeding sites; and in 1994, vaccination against *S. enteritidis* started in breeder flocks and in 1998 in layer flocks.

Linda R. Ward
John Threlfall
Henry R. Smith
Public Health Laboratory Service, Laboratory of Enteric Pathogens, Central Public Health Laboratory, 61 Colindale Avenue, London NW9 5HT, UK
Sarah J. O'Brien
Public Health Laboratory Service, Communicable Disease Surveillance Centre, 61 Colindale Avenue, London NW9 5EQ, UK

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The hypothesis posed by Bäumler *et al.*, that *S. enteritidis* is filling a niche vacated when the avian *Salmonella gallinarum* (which includes the biotypes Gallinarum and Pullorum) was eradicated from poultry populations, is intriguing, but we question whether the magnitude of *S. gallinarum* infections, even at their peak, was sufficient to impart population immunity against *S. enteritidis*. In addition, there is a disparity in time between peak prevalence of *S. pullorum* and the recent wave of occurrence of *S. enteritidis* in poultry in the United States. This recent increase of *S. enteritidis* was not detected until 1989 and was followed by a decline beginning in 1996. The wave of occurrence may be partially an artifact with geographical bias caused by disproportionate submissions from certain areas.

The role of poultry in human *S. enteritidis* infections is in itself questionable. There is little doubt that rodents were and probably still are an important reservoir of *S. enteritidis*. For almost 50 years, *S. enteritidis* was extensively used as a rodenticide in a number of European countries until 1947, and it has been suggested that this use resulted in a solid implantation of the agent in rodent populations (*1*). Rodents can be a source of *S. enteritidis* food-borne infections without the agent having passed through poultry; the presence of infected rodents in homes, nursing homes, and restaurants represents a risk for direct or indirect contamination of foods.

As pointed out by Bäumler *et al.*, an increase in human infections with *S. enteritidis* began in the 1960s, but it did not rise steadily—there was an almost 50% decrease from 1970 to 1976 (*2*). The recent increase began in 1977, with signs of a decrease beginning in 1992. In contrast, an increased frequency of *S. enteritidis* in poultry did not begin until 1989, with a decline beginning in 1996 (*3*). The reasons for the fluctuations are unknown, but there is no indication that an increased presence of *S. enteritidis* in poultry is the cause of increased food-borne infections in humans. The apparent association between the two may be due to failure in outbreak investigations to trace the agent back to its real source, which may be unrelated to poultry-containing products.

Hans Riemann
Phil Kass

Dean Cliver
Department of Population Health and Reproduction, University of California, Davis, CA 95616, USA

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Response

Our hypothesis (*1*) implies that eradication of *S. gallinarum*, including biotypes Gallinarum and Pullorum, opened an ecological niche that allowed a number of *S. enteritidis* strains to be introduced into poultry flocks from their rodent animal reservoir. Subsequently, the *S. enteritidis* strain with the highest transmissibility likely increased in frequency and eventually became predominant. In this context, it may not be surprising that PT4 was not the predominant *S. enteritidis* phage type at the beginning of the epidemic, which we hypothesized in our Perspective to have begun in the 1960s. A similar situation has been proposed for the origins of the human immunodeficiency virus (HIV) epidemic. Distinct virus strains initially entered the human population on at least seven occasions, but one strain (the HIV-1 group M virus) eventually became predominant and now accounts for most human cases (*2*). Similarly, dominant strains eventually emerged during the *S. enteritidis* epidemic, including PT4 in Europe and PT8 in the United States. However, to account for the simultaneous appearance of these different *S. enteritidis* phage types as major food-borne pathogens in Europe and the United States during the second half of the 20th century, and not before, factors that are responsible for the initial introduction of this pathogen into our egg supply need to be explored.

The point raised by Ward *et al.* that PT4 was probably introduced during the early 1980s into breeding operations may explain the accelerated epidemic spread observed in the following years. However, these data have no bearing on the origins of the epidemic because *S. enteritidis* was introduced in poultry flocks before its introduction into breeding lines. A distinction should be made between the initial introduction of *S. enteritidis* into poultry flocks from its rodent animal reservoir and factors important during the subsequent epidemic spread within the poultry industry. Although PT4 did not become the predominant human isolate in England and Wales until 1983, a steady increase of isolations was observed since the 1960s. Furthermore, at the same time an overall increase in *S. enteritidis* cases was reported from Europe and the United States, as we pointed out in our Perspective. A survey in England and Wales revealed that, in the early 1960s, *S. enteritidis* was isolated on a few occasions from egg products, but since 1967, poultry (particularly chickens) has been the only human food source in which it has been found in substantial numbers (*3*). The time marking the beginning of the steady increase in human *S. enteritidis* isolations and the time this pathogen became associated with a new food source suggest that the origins of the epidemic date back to the 1960s.

Regarding Riemann *et al.*'s letter, they suggest that rodents should be considered as a possible source for the human *S. enteritidis* epidemic. Although eggs are considered the main source of human *S. enteritidis* cases in the United States [see references in (*1*)], the possibility exists that rodents may be responsible for contaminating this food item. However, if the *S. enteritidis* epidemic would have been caused by increasing contamination of eggs with rodent feces, it would be expected that human cases with other rodent-associated *Salmonella* serotypes would also have increased during this time. For instance, *Salmonella typhimurium* and *S. enteritidis* are both isolated from rodents with similar frequencies (*4*). Although about one-third of human *S. typhimurium* cases can be traced back to chicken carcasses or eggs (*5*), the number of human cases associated with this serotype have remained almost constant during the *S. enteritidis* epidemic [see references in (*1*)]. These findings suggest that the human epidemic was caused by factors that specifically enabled *S. enteritidis*, but not *S. typhimurium*, to become more frequently associated with products from the poultry industry.

One such factor could be the loss from poultry of population immunity to the O9 antigen, which is expected to benefit *S. enteritidis* (which expresses the O9 antigen), but not *S. typhimurium* (which expresses the O4 antigen) [see references in (*1*)]. The fraction y of the susceptible poultry population that needs to be removed by disease-induced mortality or the acquisition of immunity to generate population immunity against *S. enteritidis* is a function of its basic case reproductive number, R_0, which is defined as the average number of secondary cases of infection from a primary case in a susceptible population (*6*):

$$y > 1 - 1/R_0$$

On the basis of outbreak investigations, it can be estimated that *S. gallinarum* biotypes Pullorum and Gallinarum caused at least 10% mortality in the chicken population (*7*). Surveys using the tube agglutination test (to detect the presence of anti-

body) revealed a seroprevalence of 10 to 20% (i.e., 10 to 20% of chicks had high titers of antibody) for *S. gallinarum* at the beginning of the 20th century [see references in (*1*)]. The finding that oral immunization of chickens with a *S. gallinarum* vaccine results in 60% protection but only 10% of birds react positive in the tube agglutination test can be used to calculate the fraction of immune animals from seroprevalence data (*8*). With this approach, it can be estimated that, at the beginning of the 20th century, 90% of birds survived an encounter with *S. gallinarum* and 60% of the surviving population had immunity (thus, an estimated 64% were removed from the susceptible population). Importantly, birds with immunity to *S. gallinarum* have been shown to be equally protected against colonization with *S. enteritidis* because both serotypes share the immunodominant O9 antigen (*9*). By using the above value of 0.64 for y to calculate R_0, it can be estimated that, given a basic case reproductive number for *S. enteritidis* of less than 2.8, population immunity to the O9 antigen elicited by *S. gallinarum* was sufficient to exclude *S. enteritidis* from circulation in poultry. It is likely that R_0 for *S. enteritidis* is considerably below 2.8, because even at the peak of the epidemic in 1993, this pathogen was isolated from only 7.6% of laying hens at slaughter (*10*). These theoretical considerations do not prove that eradication of *S. gallinarum* triggered the invasion of *S. enteritidis* into poultry flocks. However, our analysis suggests that *S. gallinarum* was able to competitively exclude *S. enteritidis* from circulation in poultry flocks at the beginning of the 20th century.

Andreas J. Bäumler
Department of Medical Microbiology and Immunology, Texas A&M University System Health Science Center, College Station, TX 77843–1114, USA

Billy M. Hargis[1]
Renée M. Tsolis[2]
[1]Departments of Veterinary Pathobiology and Poultry Science, [2]Department of Veterinary Pathobiology, Texas A&M University, College Station, TX 77843–4467, USA

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CORRECTIONS AND CLARIFICATIONS

News of the Week: "Start-up claims piece of Iceland's gene pie" (11 Feb., p. 951). Snorri Thorgeirsson's association with the company UVS is in a personal capacity. It should have been stated that his views expressed in the article do not necessarily represent the views of the National Cancer Institute.

Report: "Honeybee navigation: Nature and calibration of the 'odometer'" (4 Feb., p. 851). Mandyam B. Srinivasan's first name was misspelled.

Review: "Emerging infectious diseases of wildlife—Threats to biodiversity and human health" by P. Daszak *et al.* (*Science*'s Compass, 21 Jan., p. 443). The definition of BSE should have read "bovine spongiform encephalopathy," not "bovine spongiform encephalitis."