LETTERS

documented evidence about the use of the specific milk replacers, we conservatively assumed that 12 of 13 case farms used the specific milk replacers. We estimated the odds ratio for this risk factor by using logistic regression analysis. Our results indicated that the use of the milk replacers produced by the specific factory was associated with BSE infection (odds ratio [OR] 39.3, 95% confidence interval [CI] 4.9–312.9, p = 0.0005).

The milk replacers produced by the specific factory contained tallow that was produced at domestic rendering factories and imported from the Netherlands. Milk replacers were fed to calves during a relatively short period after birth (an average of 79 and 68 days, for case and control farms, respectively). If 1 production lot of milk replacer became accidentally contaminated with BSE, the exposure would occur in newborn calves within a relatively short period. This contamination may explain why 11 of 13 BSE-infected calves were born within a 2-month period from February 10, 1996, to April 8, 1996.

In Hokkaido, 9 of 10 BSE-infected calves were fed calf concentrates produced in the same feed factory. This proportion was higher than that of the 50 control farms in Hokkaido (22/50, Fisher exact test, p = 0.013). The calf concentrates might have become contaminated with meat-and-bone meal (MBM) because this factory used MBM for other animal feed. Multivariate logistic regression analysis, including this factor and that for the specific milk replacers, did not indicate significant association between the specific calf concentrates and occurrence of BSE (calf concentrates: OR 3.2 [CI 0.8–13.0], p = 0.14; milk replacers: OR 21.7 [CI 2.5–192.6], p = 0.006). The factory that provided the specific concentrates belonged to a company affiliated with the company that produced the milk replacers in question. Given the fact that farmers tend to use milk replacers and calf concentrates from the same company, association of the calf concentrates with the BSE infection may have been masked by the use of specific milk replacers. However, our study is limited by the small number of BSE cases and investigation of events that occurred 10 years ago.

A possible causal association between the feeding of potentially contaminated milk replacers to calves and the occurrence of BSE has been suggested by several epidemiologic studies (2–5). However, no report shows experimental transmission of BSE by use of tallow or milk replacers (6). This lack of evidence in the literature may suggest that the risk of contracting BSE from processed tallow or milk replacers is low (7). If MBM is excluded as a source of infection, other transmission mechanisms, such as the feeding of animal fat, may become more important.

This research was conducted under a research project for using advanced technologies in agriculture, forestry, and fisheries.

Toshiyuki Tsutsui,*
Takehisa Yamamoto,*
Sayaka Hashimoto,†
Takashi Nonaka,*
Aiko Nishiguchi,* and Sota Kobayashi*

*National Institute of Animal Health, Ibaraki, Japan; and †Headquarters, Fertilizer and Feed Inspection Services, Saitama, Japan

References

1. Hagiwara K, Yamakawa Y, Sato Y, Nakamura Y, Tobiume M, Shinagawa M, et al. Accumulation of mono-glycosylated form-rich, plaque-forming PrPSc in the second atypical bovine spongiform encephalopathy case in Japan. Jpn J Infect Dis. 2007;60:306–11.

2. Taylor DM, Woodgate SL, Atkinson MJ. Inactivation of the bovine spongiform encephalopathy agent by rendering procedures. Vet Rec. 1995;137:605–10.

3. Clauss M, Sauter-Louis C, Chaher E, Pottgiesser S, Goebel S, Selhorst T, et al. Investigation of the potential risk factors associated with cases of bovine spongiform encephalopathy in Bavaria, Germany. Vet Rec. 2006;158:509–13.

4. Jarrige N, Ducrot C, Cazeau G, Morignat E, La Bonnardiere C, Calavas D. Case-control study on feed risk factors for BSE cases born after the feed ban in France. Vet Res. 2007;38:505–16.

5. Pottgiesser C, Ovelhey A, Ziller M, Kramer M, Selhorst T, Conraths FJ. Potential risk factors associated with bovine spongiform encephalopathy in cattle from Scheswings-Holstein, Germany. J Vet Med B Infect Dis Vet Public Health. 2006;53:306–11.

6. Taylor DM, Woodgate SL, Atkinson MJ. Inactivation of the bovine spongiform encephalopathy agent by rendering procedures. Vet Rec. 1995;137:605–10.

7. European Food Safety Authority. Opinion of the Scientific Panel on Biological Hazards of the European Food Safety Authority on the “assessment of the human and animal BSE risk posed by tallow with respect of residual BSE risk.” The EFSA Journal. 2005;221:1–47 [cited 2007 May 9]. Available from http://www.efsa.europa.eu/etf/media/text/cfsa/science/biohaz/biohaz_opinions/1110.Par.0001.File.dat/biohaz_op_cj221_qra_tallow_en2.pdf

Address for correspondence: Toshiyuki Tsutsui, Epidemiological Research Team, National Institute of Animal Health, 3-1-5, Kannondai, Tsukuba, Ibaraki, 305-0856, Japan; email: tsutsui@affrc.go.jp

Control of Hepatitis A by Universal Vaccination of Adolescents, Puglia, Italy

To the Editor: The incidence of hepatitis A in Italy has decreased in the past 2 decades because of improved sanitation and better living conditions (1). However, large outbreaks occurred in the 1990s in several southern regions of Italy, despite lower rates of infection among the general popula-
tion (2–4). Person-to-person transmission has been recognized as a major factor in spread of this disease during this period (5).

Safe and highly effective hepatitis A vaccines have been available since 1995. Nevertheless, their use has been limited to the Western Hemisphere. Universal vaccination programs have been initiated only in the United States and Israel before 1998 (6). In 1998, after a large epidemic of hepatitis A, a vaccination program for toddlers and adolescents was initiated in Puglia in southeastern Italy, which has a population >4 million. This vaccine was offered free to all children 15–18 months of age and to adolescents 12 years of age. Until 2002, a combined hepatitis A plus B vaccine had been used for vaccination of adolescents as part of the national hepatitis B immunization program. In 2003, this hepatitis B vaccination program ended; only hepatitis A vaccines containing 1 antigen are now used. No catch-up vaccination campaign has been planned.

We analyzed disease surveillance and vaccine coverage data for 1991–2006 to evaluate the effect of such a vaccination program on hepatitis A incidence in persons in Puglia during the 9 years after initiation of the program. In the period before the vaccination program was initiated (1989–1997), annual incidence rates of hepatitis A in Puglia ranged from 4.3 to 139.8 cases/100,000. The average annual rate during this period was 49.5 cases/100,000. Two large outbreaks were reported in Puglia, the first in 1992 and the second in 1996–1997 (5). During the 9 years after start of the vaccination program (1998–2006), incidence of hepatitis A decreased from 22.8 cases/100,000 in 1998 to 0.7 cases/100,000 in 2006 (Figure). In the same period in other regions of Italy, incidence of hepatitis A was 5 cases/100,000, without any evident annual peak.

Since 2002, annual incidence rates in Puglia have remained at ≤2.8 cases/100,000, lower than those in the rest of Italy. This incidence has been observed in all age groups, without any differences between vaccinated and unvaccinated birth cohorts. Vaccination coverage among children 15–18 months of age was <20% during the period of the vaccination program. Coverage levels in adolescents reached 65% in the third year after the start of the program and then ranged from 57% to 72% (Figure).

Hepatitis A has been a serious public health problem in Puglia. This disease has had a detrimental effect on the local economy, which is based on tourism and trade of food products. However, since the vaccination program was started in 1998, disease incidence has decreased. During the study period, no other alternative prevention measures that could have had an effect on disease control were implemented.

High levels of vaccination coverage have not been achieved since the start of the campaign, and no catch-up vaccination program has been implemented. The decrease in hepatitis A incidence we observed involved all age groups, including those not covered by the vaccination program. This finding may indicate strong herd immunity, which would confirm what has been observed in other countries (7–9). However, there is uncertainty in interpreting current epidemiologic data. On the basis of available data, we cannot assess whether the current low incidence of hepatitis A in Puglia is caused by vaccination alone or in combination with other factors. We also cannot exclude the possibility that what we observed may have been an interepidemic period and that new episodes may occur in the future.

Our results indicate that local health authorities should be aware of possible increases in the incidence of hepatitis A in Puglia. An urgent catch-up vaccination program may be necessary to prevent future outbreaks. Moreover, a seroepidemiologic survey would be useful for assessing the size of the susceptible population and most vulnerable age groups.

Pietro Luigi Lopalco,* Rosa Prato,† Maria Chironna,* Cinzia Germinario,* and Michele Quarto*  
*University of Bari, Bari, Italy; and †University of Foggia, Foggia, Italy

References

1. D’Amelio R, Mele A, Mariano A, Romanò L, Biselli R, Lista F, et al. Hepatitis A, Italy [letter]. Emerg Infect Dis. 2005;11:1155–6.
2. Moschen ME, Floreani A, Zamparo E, Baldo V, Majori S, Gasparini V, et al. Hepatitis A infection: a seroepidemiological study in young adults in north-east Italy. Eur J Epidemiol. 1997;13:875–8.

---

Figure. Incidence of hepatitis A in Puglia, Italy (gray line) compared with the rest of Italy (black line), 1998–2006, and hepatitis A vaccination coverage among adolescents in Puglia (dashed line), 1998–2005.
Address for correspondence: Pietro Luigi Lopalco, Universita’ di Bari, Policlinico, Piazza Giulio Cesare, 70124 Bari, Italy; email: p.lopalco@igiene.uniba.it

Human
Rickettsia sibirica mongolitimonae
Infection, Spain

To the Editor: Rickettsia sibirica mongolitimonae has been recently reported as a subspecies of R. sibirica (1). The first evidence of R. sibirica mongolitimonae pathogenicity in humans was documented in France in 1996 (2). Since then, 11 more cases in France, Algeria, South Africa, Greece, and Portugal have been reported (3–6). Because the main clinical manifestations include lymphangitis, the acronym LAR (lymphangitis-associated rickettsiosis) has been proposed (3). We report a case from Spain that confirms the broad distribution of this agent in southern Europe.

A 41-year-old man was admitted on June 19, 2007, to the Hospital de Cruces (Baracaldo, Spain) with fever (39°C), malaise for a week, sweating, lumbar and knee pain, disseminated myalgias, and headache. He reported that 20 days before admission he had removed an engorged tick from his right leg while working as a topographer in the Balmaseda Mountains, 30 km from Bilbao. He had also removed several ticks from his body 4 days before the onset of symptoms. Physical examination did not demonstrate relevant findings. There was no inoculation eschar at the tick-bite sites. Rash, lymphadenopathies, and lymphangitis were not observed.

Chest radiograph did not show consolidation or other abnormality. Initial laboratory examination, on June 21, 2007, showed a leukocyte count 5.2 × 10³/μL, hemoglobin 14.1 g/dL, platelet count 190,000/μL, erythrocyte sedimentation speed 9 mm/h, urea 38 mg/dL, creatinine 0.9 mg/dL, aspartate aminotransferase 229 IU/L, alanine aminotransferase 170 IU/L, alkaline phosphatase 158 IU/L, gamma-glutamyl-transpeptidase 111 IU/L, total bilirubin 1.3 mg/dL, and C-reactive protein 4.3 mg/dL. Because the patient had been bitten by a tick, acute-phase serum and EDTA-treated blood samples were sent to the Special Pathogens Laboratory (Área de Enfermedades Infecciosas – Hospital San Pedro from La Rioja), where a presumptive diagnosis of rickettsiosis was made. On June 22, 2007, treatment with doxycycline was begun (100 mg/day for 12 days), and his condition rapidly improved.

The early-phase serum yielded low immunoglobulin (Ig) G titer (<64) against Rickettsia conorii and Anaplasma phagocytophilum antigens, and results of ELISA and Western blotting for Lyme borreliosis were negative. A convalescent-phase serum sample collected 7 weeks later did not contain IgG antibodies against spotted fever group Rickettsia species when R. conorii antigen was used.

DNA was extracted from the early whole-blood specimen by using QIAamp DNA Blood minikit (QIAGEN, Hilden, Germany) according to the manufacturer’s instructions. This DNA extract was used as template in nested PCR assays targeting the spotted fever group rickettsial ompB (420 bp) and gltA (337 bp) genes (7). Quality control included both positive (with R. conorii Malish #7 grown in Vero cells) and negative controls that were extracted and PCR amplified in parallel with the specimens. Negative controls consisted of sterile water instead of template DNA. Amplification products of the expected size were obtained. The sequences of these amplicons allowed the identification of R. sibirica mongolitimonae with 99.5% and 100% similarity for ompB and gltA, respectively (GenBank accession nos. DQ097083 and DQ097081).

To our knowledge, Rickettsia species have never been detected in ticks or human specimens in Spain. The host ticks of this rickettsia are likely Hyalomma species, which are more prevalent in southern Spain. In our region in northern Spain, Hyalomma marginalatum represented 8% of ticks that fed on humans during 2001–2005, although an increase in this number was recorded last year (data not shown).

In our patient, Rickettsia’s pathogenic role was demonstrated by PCR, a technique that has previously enabled us to identify other arthropod-borne Rickettsia species (8,9). This case suggests that R. sibirica mongolitimonae infection should be considered in the differential diagnosis of rickettsiosis and tick-bite febrile patients in Spain and confirms the distribution of this rickettsia in southern Europe. According to the literature (3), some patients in whom R. sibirica mongoli-