What is already known on this topic?

Since the 1960s, 6 to 9 months of isoniazid (INH) has been the mainstay of treatment for latent tuberculosis infection (LTBI), but its application has been limited by concerns about the toxicity of isoniazid and the long duration of treatment.

What is added by this report?

During 2004–2008, a total of 17 serious liver injuries were reported in patients receiving INH therapy; five patients underwent liver transplantation, and five died, including one liver transplant recipient.

What are the public health implications for public health practice?

Patients receiving INH therapy for LTBI should be told categorically by medical providers to stop taking their medication immediately if they have symptoms such as nausea, vomiting, abdominal discomfort, or unexplained fatigue and to contact their providers for further evaluation.

Multistate Outbreak of Human Salmonella Typhimurium Infections Associated With Pet Turtle Exposure—United States, 2008

ON SEPTEMBER 4, 2008, THE PHILADELPHIA Department of Public Health (PDPH) and the Pennsylvania Department of Health (PADOH) notified CDC of an outbreak of possible turtle-associated human Salmonella Typhimurium infections detected by identifying strains with similar pulsed-field gel electrophoresis (PFGE) patterns in PulseNet. Turtles and other reptiles have long been recognized as sources of human Salmonella infections,1 and the sale or distribution of small turtles (those with carapace lengths <4 inches) has been prohibited in the United States since 1975.2 CDC and state and local health departments conducted a multistate investigation during September—November 2008. This report summarizes the results of that investigation, which identified 135 cases in 25 states and the District of Columbia; 45% were in children aged ≤5 years. Among 70 patients with primary infection, 37% reported turtle exposure, of which 81% was to small turtles most commonly purchased from street vendors. A matched case-control study showed a significant association between illness and exposure to turtles (matched odds ratio [mOR] = 16.5). Increasing enforcement of existing local, state, and federal regulations against the sale of small turtles, increasing penalties for illegal sales, and enacting more state and local laws regulating the sale of small turtles (e.g., requiring Salmonella awareness education at the point-of-sale),

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10 Available.

*isonicotinylhydrazine.
†Monthly clinical monitoring (including a physical examination) for the signs and symptoms of adverse events is recommended by ATS and CDC for all LTBI treatment patients.1,2 Existing guidelines suggest that patients who have HIV infection, patients who have chronic liver disease, pregnant women, women in the immediate postpartum period (≤3 months of delivery), and patients who use alcohol regularly should be considered for baseline laboratory hepatic testing. Routine laboratory testing is indicated for patients whose baseline testing is abnormal and other persons at risk for hepatic disease.1,2

†Predictors of INH-associated liver injury include pre-existing liver disease, HIV infection, injection-drug use, concurrent alcohol consumption, pregnancy or the immediate postpartum period (≤3 months of delivery), concomitant administration of medications with hepatotoxic potential, and older age.1,2

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could augment federal prevention efforts.

On July 9, 2008, a girl aged 2 years was brought to a Philadelphia physician’s office after 3 days of diarrhea and fever. S. Typhimurium was isolated from her stool specimen. Three weeks before her illness began, the family had purchased two pet turtles with shell lengths <4 inches from a street vendor. The family reported that the child did not touch the turtles but touched the turtle aquarium. On July 28, PulseNet* was notified that stool specimens from five additional Pennsylvania patients yielded S. Typhimurium with a PFGE XbaI pattern indistinguishable from the girl’s isolate (JPXX01.0416) or different by a single band (JPXX01.0006). Each of these PFGE patterns had been observed previously and comprised 1.1%-1.2% of the PulseNet Salmonella database. By mid-August, PulseNet had identified S. Typhimurium isolates matching the outbreak strain in 10 states.† Concomitantly, epidemiologic investigations led by PDPH and PADOH revealed that five of eight Philadelphia patients and two additional Pennsylvania patients reported exposure to a turtle in household settings.

**Multistate Investigation**

On September 4, 2008, after a turtle aquarium water sample from a Philadelphia patient’s home was positive for the outbreak strain, CDC and state and local health partners initiated a multistate investigation to determine the source of infections. A case was defined as a laboratory-confirmed infection of S. Typhimurium with the outbreak strain (PFGE XbaI pattern JPTX01.0416 or JPTX01.0006) in a person with an illness onset date on or after March 13, 2008 (earliest reported illness onset date). A case of secondary infection (secondary case) was defined as illness in a person occurring within 2 weeks after diarrheal illness in a household or day care contact, suggesting person-to-person transmission. All cases that were not identified as secondary cases were classified as primary cases.

A total of 135 cases in 25 states and the District of Columbia were identified in the national PulseNet database. Among 124 patients for whom demographic information was available, median age was 7 years (range: <1-94 years), and 54 (45%) patients were aged ≤5 years; 63 (51%) were female. Reported illness onset dates ranged from March 13 to October 7; 78% of illnesses occurred during June—September.

Eighty-three (61%) of 135 patients were interviewed using a more extensive questionnaire that asked about clinical symptoms, day-care attendance, reptile exposure (turtle size, species, acquisition source, and type and extent of turtle contact), and awareness of the association between reptile contact and Salmonella infection. Of the 83 patients, 35 (42%) had bloody diarrhea, and 29 (35%) were hospitalized; no deaths were reported. Twenty (24%) of 83 patients attended day care. Nine of those 20 children attended three Pennsylvania day-care centers, and they acquired secondary Salmonella infections through contact with laboratory-confirmed index cases, one in each day-care center. All the index patients acquired their infections through turtle exposure, and all 12 children were aged <2 years. Investigators classified 70 of the 83 interviewed patients as having primary cases and 13 (16%) as secondary cases. The median age of these 70 patients was 8 years (range: <1-80 years); 43% were aged <5 years, and 36 (51%) were female. Of the 70 patients with primary cases, 26 (37%) reported exposure to turtles, and 21 reported exposures to small turtles. Among the 69% of patients who knew the source of the turtle, the majority of turtles were purchased from street vendors, flea markets, and nonpet stores (e.g., souvenir and gift shops). Seven (10%) of 70 primary patients reported other reptile exposures (e.g., snakes or iguanas). Three of six water samples from turtle habitats in patient households yielded the outbreak strain.

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**Box. Existing recommendations to prevent turtle-associated Salmonella infections**

- Do not have a turtle in any household that includes children aged <5 years, the elderly, or persons who have lowered natural resistance to disease due to pregnancy, cancer, chemotherapy, organ transplants, diabetes, liver problems, or certain other diseases. A family expecting a child should remove any pet reptile or amphibian from the home before the infant arrives.
- Wash hands thoroughly with soap and water immediately after handling turtles or their cages, or after contact with pet feces. Do not touch your face, other persons, or any surface until hands are washed.
- Handle all turtles and surfaces that have come in contact with turtles as if they are contaminated with Salmonella, because they likely are.
- Wash surfaces that the turtle or its cage has contacted. Kitchen sinks should not be used to bathe turtles or to wash their dishes, cages, or aquariums. If bathtubs are used for these purposes, they should be cleaned thoroughly and disinfected with bleach before use.
- Separate the turtle from possible contact with food intended for humans. Do not allow turtles to roam freely about a home or living area, and especially do not allow them in food preparation areas. Do not allow food and drink to be present in animal contact areas. Do not use kitchen sinks to bathe turtles or to wash their dishes, cages, or aquariums. If bathtubs are used for these purposes, they should be cleaned thoroughly and disinfected with bleach.

Source: CDC. Is a turtle the right pet for your family? Available at http://www.cdc.gov/healthypets/spotlight_an_turtles.htm.
During September 18–October 10, 2008, a nationwide 1:1 matched case-control study was conducted to identify whether illness was associated with exposure to turtles or other reptiles. Data were collected through telephone interviews by local, state, and CDC epidemiologists using the outbreak questionnaire. For the case-control study, only primary cases with illness onset (or date of isolation of the outbreak strain, if the onset date was unknown) on or after March 13, 2008, were eligible. Controls were persons without diarrheal illness during August and were matched by case neighborhood (using reverse directory dialing) and age group (i.e., <1 year, 1-5 years, 6-17 years, ≥18 years). The questionnaire asked about history of reptile exposure for the week preceding illness onset for case-patients and during August for controls. Investigators chose August for controls to help decrease recall bias, reasoning that, without illness to delineate clearly a time period, controls might have more difficulty recalling the timing of exposures.

Thirty-seven cases and 47 controls were enrolled from 11 participating states. A total of 33 cases could not be enrolled in the case-control study because of refusal to participate, loss to follow-up, or inability to identify a matching control. Six cases had more than one matched control enrolled, and these were included in the analysis to increase study power. The median age of case-patients was 9 years (range: 1-80 years), compared with 14 years (range: 1-90 years) for controls (p=0.44); 51% of case-patients were female, compared with 40% of controls (p=0.34). Eighteen (49%) of 37 case-patients reported turtle exposure, compared with nine (19%) of 47 controls (mOR=16.5). Sixteen (94%) of the 17 case-patients for whom information was available had exposure to a turtle with shell length <4 inches. Illness was not associated with exposure to nonturtle reptiles.

On October 20, 2008, PDPH issued a health advisory informing the public about the outbreak and providing recommendations for preventing illness. Attempts to trace back the source of the infected turtles were unsuccessful, partly because street or flea market vendors move frequently, complicating investigation efforts. In November 2008, the Food and Drug Administration reemphasized its warning to consumers against buying small turtles.

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CDC Editorial Note: This S. Typhimurium outbreak is the third multistate, turtle-associated Salmonella outbreak in the United States since 2006. Before 2006, no large multistate turtle-associated Salmonella outbreaks were identified. One reason for this apparent increase might be PulseNet, which has improved the ability to detect multistate outbreaks. Increased pet turtle ownership in the United States also might contribute to the recurrent outbreaks: the proportion of households in the United States owning pet turtles doubled during 1996-2006, from 0.5% to 1.0%.

Together, the three recent Salmonella outbreaks account for 258 laboratory-confirmed cases of salmonellosis and many more unreported illnesses likely occurred. As with past outbreaks, most ill persons reporting turtle exposure were exposed to turtles with shell lengths <4 inches; these turtles were mainly acquired from flea markets, street vendors, and souvenir shops. The case-control study found a significant association of Salmonella infection with turtle exposure; however, 63% of primary cases in the outbreak had no known turtle exposure, and 60% had no reptile exposure. This might have resulted, in part, from failure to recall a turtle exposure. Parents or guardians were interviewed as proxies for young children, and they might have been unaware of their child’s turtle exposure outside of the home. In addition, certain patients might have had unknown indirect turtle exposure through environmental cross-contamination or unrecognized person-to-person transmission or have been sporadic or background cases.

The federal government prohibited sales of turtles with shell lengths <4 inches in 1975, after investigations demonstrated that small turtles were a major source of human Salmonella infections, particularly in children; despite this, outbreaks of Salmonella infection continue to be linked to these small turtles, in part due to illegal sales.

What is already known on this topic?

A federal prohibition against sales of turtles with shell lengths <4 inches was enacted in 1975, after investigations demonstrated that small turtles were a major source of human Salmonella infections, particularly in children; despite this, outbreaks of Salmonella infection continue to be linked to these small turtles, in part due to illegal sales.

What is added by this report?

This report documents the third multistate Salmonella outbreak in the United States since 2006 associated with turtles, primarily those turtles with shell lengths <4 inches that were acquired through illegal sales; it also highlights that young children without direct turtle exposure are at risk for turtle-associated salmonellosis through person-to-person transmission in child-care settings.

What are the implications for public health practice?

Increasing enforcement of existing local, state, and federal regulations against the sale of small turtles, increasing penalties for illegal sales, and enacting more state and local laws regulating the sale of small turtles (e.g., requiring Salmonella awareness education [see Box at the point-of-sale], could augment federal prevention efforts and facilitate a more rapid public health response.

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in U.S. children. However, because the prohibition is not fully enforced and contains exceptions (e.g., sales for bona fide scientific, educational, or exhibition purposes), turtle-associated human salmonellosis cases continue to occur. Street vendors and flea markets are a common source of illegal sales; these were common sources reported in this outbreak.

Despite recommendations from CDC to prevent turtle-associated salmonellosis in humans (see Box), recent outbreaks suggest public education efforts have not been successful. In this outbreak, <30% of respondents knew about the association between reptiles and Salmonella; this proportion has not increased substantially compared with the 20%-29% observed in the 2007-2008 outbreak. Although many reptiles carry Salmonella, small turtles pose a greater risk to young children because they are perceived as safe pets, are small enough to be placed in the mouth, or otherwise can be handled inappropriately. Persons having contact with reptiles, reptile habitats (including tank water), and other surfaces contaminated with reptile feces are at risk for Salmonella infection; direct reptile contact is not necessary. This outbreak documents that young children without direct turtle exposure are at risk for turtle-associated salmonellosis through person-to-person transmission in child-care settings. Direct or indirect reptile contact is associated with an estimated 6% of Salmonella infections in the United States and 11% of infections among persons aged <21 years.

Because of the particular hazard associated with small turtles, continuing federal prohibition against sales and distribution of small turtles is needed to prevent turtle-associated salmonellosis. Few states have laws regulating small turtles, and most of these laws prohibit turtles in day-care centers or require sellers to provide educational material. Increasing enforcement of existing local, state, and federal regulations against the sale of small turtles, increasing penalties for illegal sales, and enacting more state and local laws regulating the sale of small turtles (e.g., requiring Salmonella awareness education at the point-of-sale), could augment federal prevention efforts and facilitate a more rapid public health response.

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* A national molecular subtyping network for foodborne disease surveillance.
†Alabama, Illinois, New York, Ohio, Oklahoma, Pennsylvania, South Dakota, Texas, Vermont, and Virginia.
‡ Date of outbreak strain isolation minus 3 days (account for the incubation period of Salmonella) was used to estimate illness onset date if that date was unknown.
¶ Available at http://www.fda.gov/forconsumers/consumerupdates/ucm04B081.htm.
¶¶ Also available at http://www.cdc.gov/healthypets/spotlight_an_turtles.htm.

In 2006, a total of 26,389 deaths from unintentional drug poisoning occurred in the United States, with the national age-adjusted death rate more than doubling since 1999, from 4.0 to 8.8 per 100,000 population. Opioid pain medications were involved in more than half of the drug poisoning deaths in 2006 in which a drug was specified.

On March 18, 2010, CDC released an issue brief, Unintentional Drug Poisoning in the United States, summarizing the most recent information regarding deaths and emergency department visits resulting from drug overdoses. That brief includes information on overdose trends, the most common drugs involved, and the regions and populations most severely affected. Recommendations on how health-care providers, private insurance providers, and state and federal agencies can work to prevent unintentional drug overdoses are also included. The issue brief is available at http://www.cdc.gov/homeandrecreationsafety/poisoning/activities.htm.

Additional educational resources regarding poisoning prevention are available from CDC at http://www.cdc.gov/homeandrecreationsafety/poisoning/index.html and http://www.cdc.gov/features/medicsafety. The national toll-free telephone number for poison-control centers is 1-800-222-1222.

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