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Abstract: Abstract Reptile-associated salmonellosis (RAS) in children has been reported primarily due to direct contact with turtles, but recently also due to indirect contact with more exotic reptiles, causing disease in infants. To evaluate risk factors for RAS, we reviewed the RAS cases published in the literature since 1965. A case was defined as a child 18 years of age with an epidemiological link by identification of Salmonella enterica in cultures from both the affected child and the exposed reptile. We identified a total of 177 otherwise healthy children (median age 1.0 years, range 2 days to 17.0 years). RAS manifested mainly with gastrointestinal disease, but 15% presented with invasive RAS, including septicemia, meningitis, and bone and joint infection. The children with invasive RAS were significantly younger than children with noninvasive disease (median age 0.17 and 2.0 years, p<0.0001). RAS is most frequently seen after exposure to turtles (42%). However, children with invasive RAS had been exposed more often (p 0.001) to reptiles other than turtles, including iguanas, bearded dragons, snakes, chameleons, and geckos. Children exposed to those latter reptiles usually kept indoors were younger than children exposed to turtles mostly kept outdoors (p<0.0001). RAS in children is significantly associated with invasive disease at young age, in particular infants <6 months of age. Exposure to reptiles, other than turtles, kept indoors is associated with RAS at younger age and more invasive disease. This finding is helpful for recognizing or even preventing invasive RAS in young infants that are at highest risk.

DOI: https://doi.org/10.1089/vbz.2012.1133

VECTOR-BORNE AND ZOONOTIC DISEASES
Volume 13, Number 6, 2013

DOI: 10.1089/vbz.2012.1133

Risk Factors for Invasive Reptile-Associated Salmonellosis in Children

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Abstract

Reptile-associated salmonellosis (RAS) in children has been reported primarily due to direct contact with turtles, but recently also due to indirect contact with more exotic reptiles, causing disease in infants. To evaluate risk factors for RAS, we reviewed the RAS cases published in the literature since 1965. A case was defined as a child ≤18 years of age with an epidemiological link by identification of *Salmonella enterica* in cultures from both the affected child and the exposed reptile. We identified a total of 177 otherwise healthy children (median age 1.0 years, range 2 days to 17.0 years). RAS manifested mainly with gastrointestinal disease, but 15% presented with invasive RAS, including septicemia, meningitis, and bone and joint infection. The children with invasive RAS were significantly younger than children with noninvasive disease (median age 0.17 and 2.0 years, $p < 0.0001$). RAS is most frequently seen after exposure to turtles (42%). However, children with invasive RAS had been exposed more often ($p \leq 0.001$) to reptiles other than turtles, including iguanas, bearded dragons, snakes, chameleons, and geckos. Children exposed to those latter reptiles usually kept indoors were younger than children exposed to turtles mostly kept outdoors ($p < 0.0001$). RAS in children is significantly associated with invasive disease at young age, in particular infants <6 months of age. Exposure to reptiles, other than turtles, kept indoors is associated with RAS at younger age and more invasive disease. This finding is helpful for recognizing or even preventing invasive RAS in young infants that are at highest risk.

Key Words: *Salmonella enterica*—Salmonellosis—Reptile—Reptile-associated salmonellosis—Invasive infection—Children.

Introduction

Reptile-associated salmonellosis (RAS) is being recognized as an emerging zoonosis (Mermin et al. 2004) and is consistently associated with invasive disease (Mermin et al. 1997). A 7-week-old girl with invasive *Salmonella* infection due to exposure to family's pet bearded dragon (see Supplementary Data File 1; Supplementary Data are available at www.liebertonline/vbz/) and the recent article by Weiss et al. (2011) reporting RAS cases due to indirect contact between babies and bearded dragons prompted us to evaluate risk factors for RAS in children reported in the literature. The aim of this report is to provide an analysis of published data and risk factors regarding invasive manifestations of RAS in children.

Materials and Methods

We reviewed all published cases of RAS in children. A case was defined as a child ≤18 years of age with an epidemiological link by identification of *Salmonella enterica* (hereafter referred to as *Salmonella*) in cultures from both the affected child and the exposed reptile (and/or its environmental contamination) between 1965 and July, 2012 (see Supplementary Data Files 2 and 3).

Results

We identified 182 cases of RAS (including our case). Of these, 177 children were otherwise healthy, whereas 5 suffered from immunocompromising co-morbidity (including

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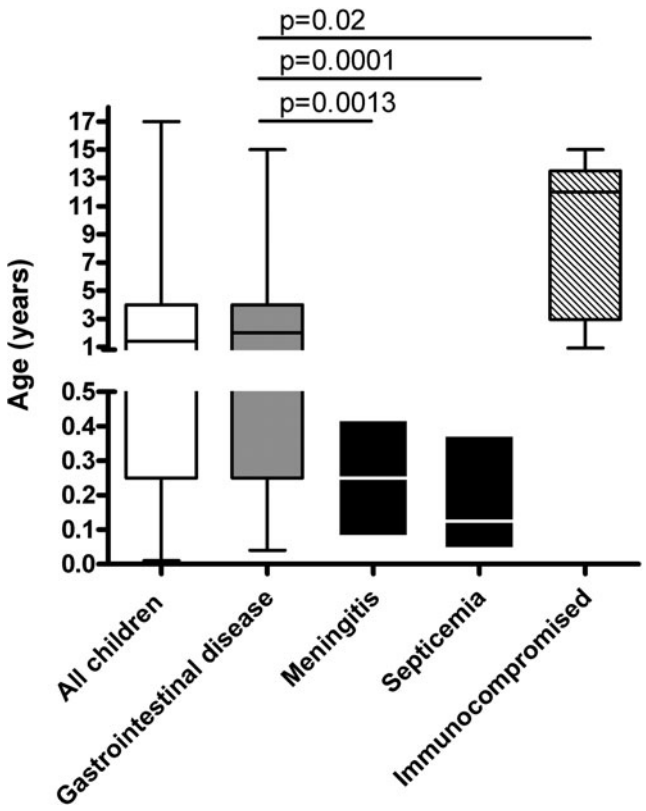

FIG. 1. Age-related manifestations of RAS in children: Box and whisker plots with the median, the interquartile ranges (box), and 10th and 90th percentiles (bars).

lymphocytic leukemia, glioma, hepatoblastoma, systemic lupus erythematosus, and 1 not further defined immunodeficiency). RAS manifested mostly with gastrointestinal disease ($n = 139/177$; 78%), but 15% presented with invasive RAS including septicemia ($n = 14$), meningitis ($n = 9$), and bone and joint infection ($n = 3$). Four children were asymptomatic, and disease manifestation was not reported in 8 children. Data on the age of individual patients were available from 121 otherwise healthy children: The median age was 1.0 years (mean 2.7, range 2 days to 17.0 years); almost half of the children (49%) were <1 year and 81% <5 years of age, respectively. Children with invasive RAS ($n = 26$; median age 0.17 years) were younger than children with noninvasive disease (median age 2.0 years, $p < 0.0001$) (Fig. 1).

All isolated *Salmonella* belonged to the species *enterica*, predominantly to the subspecies I (*enterica*, 163 cases, 90%), but also to subspecies IIIa (*arizonae*, 9 cases) and IV (*houtenae*, 10 cases). Exposure to turtles was the predominant reptile exposure overall (42%; 75/177) and in children with gastrointestinal disease (45%; 63/139). In contrast, exposure to iguanas was significantly more prevalent in children with invasive disease ($p \leq 0.001$), *i.e.*, septicemia (7/14; 50%) or meningitis (6/9; 67%). As exposure to iguanas caused significantly more invasive RAS and to turtles more gastrointestinal RAS, we compared patients' age with the kind of reptile exposure: Children with exposure to reptiles kept indoors (*e.g.*, iguanas, bearded dragons, snakes, chameleons, and geckos) were younger (median age 0.3 years, 80% of patients <1 year of age) than children exposed to turtles which may be kept also outdoors (median age 3.0 years, 20% of patients <1 year of age) ($p < 0.0001$) (Fig. 2).

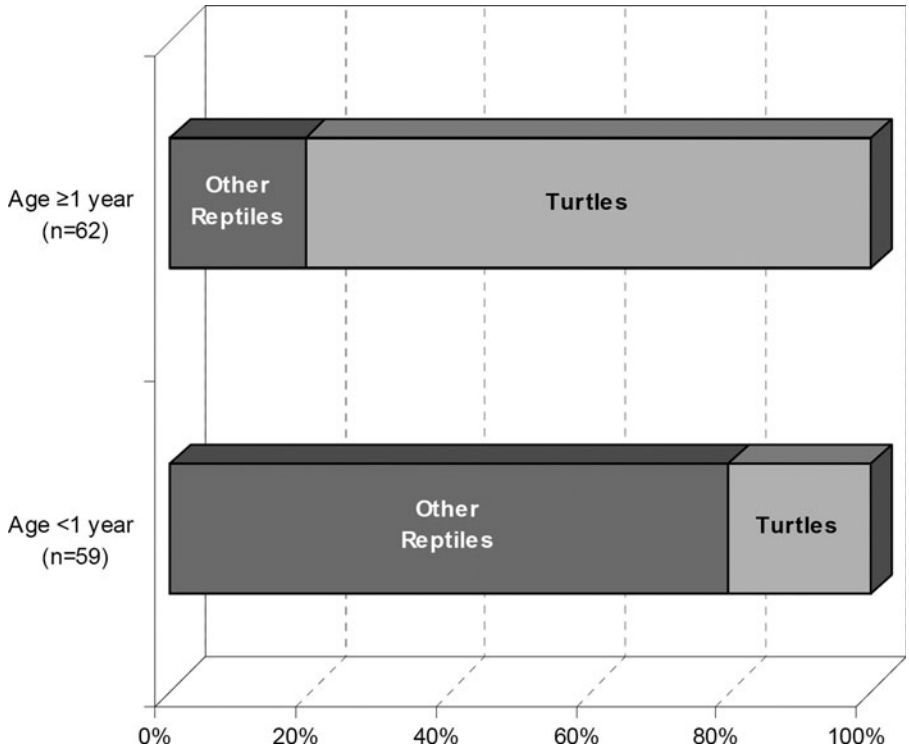

FIG. 2. Reptile exposure in children with RAS divided into two age groups: <1 year and ≥1 year. Children with exposure to turtles mostly kept outdoors were older (81% ≥1 year) than children exposed to other reptiles kept indoors ("other reptiles": *e.g.*, iguanas, bearded dragons, snakes, chameleon, geckos; 80% <1 year).

Discussion

The present data analysis clearly demonstrates the significant association of RAS with invasive disease at young age, in particular infants <6 months of age. Moreover, we disclose for the first time that exposure to reptiles kept indoors is significantly associated with RAS at younger ages and with more invasive disease.

Invasive *Salmonella* infections, including septicemia and meningitis, are accumulated in very young children and the immunocompromised host, including human immunodeficiency virus (HIV) infection (Gordon et al. 2008). Both antibodies and complement are needed for phagocytosis, oxidative burst function, and cellular killing of *Salmonella* by macrophages in the human host (MacLennan et al. 2008, Gondwe et al. 2010). Indeed, a lack of *Salmonella*-specific antibodies was found in African children <2 years of age and was linked not only epidemiologically to nontyphoidal *Salmonella* bacteremia (MacLennan et al. 2008), but also to lower induction of neutrophil oxidative burst (which correlates with killing of *Salmonella*) (Gondwe et al. 2010). Thus, these findings may help to explain why young children are essentially prone to invasive *Salmonella* infections, including bacteremia, sepsis, meningitis, and death (Mermin et al. 2004).

In addition to the young age, we found another significant risk factor for RAS, which is exposure to reptiles kept indoors, *e.g.*, iguanas, bearded dragons, snakes, chameleons, and geckos. The potential source of *Salmonella* in these reptiles is the common environmental contamination by reptile feces (Mitchell and Shane 2000), in which *Salmonella* is expected to survive over months (Morse and Duncan 1974) and which is thought to be the source for eventual horizontal transmission.

Two reasons may be considered for the higher prevalence of RAS with reptiles kept indoors:

1. The colonization occurs already early in life in hatchlings due to contact with soil or eggshell remnants (Mitchell and Shane 2000). The risk of transmission is increased in young reptiles kept indoors, living, *i.e.*, in breeding farms and pet shops, where a high diversity and number of animals are kept in close contact (Mitchell and Shane 2000). One might speculate that for this reason these reptiles harbor and can shed more *Salmonella* organisms than turtles (Geue and Loschner 2002) and frequently carry multiple *Salmonella* strains in a saprophytic state (Ward 2000, Willis et al. 2002). Therefore, the identification of different serovars (or strains) in reptiles and children does not exclude the reptile as a source of infection (Weiss et al. 2011), as this was the case in 9 reports including our patient.
2. The higher frequency of RAS with reptiles kept indoors may be that purchased reptiles kept indoors are in closer direct and indirect contact with the family members in the household. Moreover, they may have free access to areas in the house where infants live in close direct or indirect contact (*e.g.*, by crawling and oral exploration). Horizontal transmission of *Salmonella* between these pets and infants directly or indirectly by other caretaking household members not adhering to handwashing or contaminated household objects therefore must always be considered (Weiss et al. 2011).

In conclusion, this report demonstrates significant risk factors for invasive RAS in children and re-emphasizes that parents should be informed about the risk of RAS to their infants, even by indirect contact to reptiles kept indoors. The well-described behavior rules for primary prevention (Mermin et al. 2004) need to be reinforced.

Author Disclosure Statement

No competing financial interests exist.

P.M.M.S., C.R., M.H., and C.B. managed the patients; M.M.W. did expert consultation on microbiologic analyses; and P.M.M.S., C.R., M.H., and C.B. wrote the manuscript. All authors commented on the final manuscript. The authors have no conflicts of interest to disclose.

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