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Shigellosis due to occupational contact with non-human primates

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SUMMARY

A small cluster of dysenteric illness, due to *Shigella flexneri*, was identified among technical assistants of a primate research unit. All of the affected individuals had been in regular contact with a colony of cynomolgus macaque monkeys, one of which was known to have suffered from acute haemorrhagic colitis in the preceding few weeks. Four monkeys were found to be excreting *S. flexneri* bacilli of identical antigen type (1b) to that isolated from the human cases. Investigation of working practices revealed the potential for inadvertent faeco-oral spread and the need to improve existing control methods. We conclude that this small outbreak of shigellosis represents a primate-associated occupational zoonosis. The risk may not be fully appreciated by handlers or their doctors.

INTRODUCTION

Primates may be affected by a number of zoonotic agents, some of which can cause serious illness in Man; herpes virus simiae (the 'B' virus) is well-known [1]; but the risk from enteric organisms is, perhaps, less well-recognized and probably underestimated. The gastrointestinal tract of primates may carry *Salmonella*, *Campylobacter*, *Entamoeba* and *Giardia* species [2], as well as those of the *Shigella* genus.

Shigella infection of non-human primates has been recognized since the early part of this century [3] (although Man provides the natural reservoir of infection) and shigella infection of laboratory colonies of non-human primates has been identified in the UK [4, 5]. There have been a few reports in the past of human shigella infection related to contact with pet or zoo primates [6–8].

An investigation was mounted after complaints of diarrhoea were reported by research staff who had been in regular contact with cynomolgus monkeys (*Macaca fascicularis*). One monkey had suffered from acute haemorrhagic colitis 3 weeks prior to the onset of symptoms in the employee first affected. Post-mortem

examination had revealed ulceration of the stomach and caecum, and histopathological opinion suggested 'parasitism' as the cause of the disease.

SUBJECTS, MATERIALS AND METHODS

The primate house was visited and staff observed at work. Attention was directed to animal-handling procedures, control of contaminated aerosols, cleaning practices, hygiene standards and the quality of protective clothing provided.

Medical histories were obtained from each of the symptomatic employees. Those absent through sickness were seen at home. Stool specimens were provided by each of the affected individuals, their family members and close social contacts. MacConkey and deoxycholate–citrate–lactose–sucrose agar was used as the culture medium. Isolates were identified biochemically by the API system 20E (Biomérieux, Basingstoke, Hants, UK) and by slide agglutination with shigella antiserum.

Stool specimens were obtained from a sample of 87 macaques from a varying total population of about 180 to give a representative cross-section from different sources of supply. Specimens were examined in the laboratory using a variety of bacteriological media [9]. Faeces were plated onto MacConkey and deoxycholate citrate agar and a portion was put in Selenite F medium. After 24 h incubation at 37 °C the plates were examined for the presence of non-lactose or weakly-lactose fermenting colonies. Sub-cultures were made from the selenite broth onto further MacConkey and deoxycholate agar plates which were treated as before. Colonies were sub-cultured onto horse blood agar and pure colonies were identified. In addition, the faeces were cultured onto blood agar anaerobically and onto campylobacter-selective agar. Several identification methods were combined, these being the API systems of Rapidec Z, API 10S and API 20E. If the results of the tests indicated shigella, serological tests were carried out using slide agglutination with antisera (Wellcome Diagnostics Ltd, Kent, UK) and tube agglutination using a heat-treated antigen suspension.

RESULTS

Three employees complained of passing loose, blood-streaked motions accompanied by mucous discharge, loss of appetite and, in two cases, weight loss of about 6 kg. Illness durations in the three cases were 30, 8 and 18 days. One individual required hospitalization for intravenous rehydration. None received antibiotic therapy, and all made a full recovery. Time interval between onset of symptoms for first and second cases was 20 days, and for second and third cases 12 days.

A further two employees working in the primate house reported recent diarrhoeal illnesses, but had fully recovered by the time of investigation.

None of the affected workers reported a history of travel abroad in the preceding few weeks. One individual had been on holiday in Turkey 5 months previously but had suffered no illness at that time, nor on subsequent return to this country.

Workplace inspection and evaluation suggested that faecally-contaminated aerosols could be created during hose-cleaning of the primate house. Blood-stained

mucoid material was observed in excrement-collecting trays sited below cages and considered by the company veterinary surgeon to be of enteric, rather than menstrual, origin. The atmosphere of the house was maintained under negative pressure and mechanically ventilated to ensure 15 air changes per hour.

Direct contact with the animals was required during experimental procedures requiring manual restraint. Protective clothing was worn by employees, including a disposable, facepiece respirator. Staff changing facilities did not have well-demarcated 'clean' and 'dirty' areas.

Shigella flexneri was isolated by culture of stool specimens provided by each of the three individuals affected at the time of the investigation. The isolate was identified as the 1b serotype. No other pathogens were identified by microscopy or culture. Specimens from the other two employees reporting recent bowel upset, but who were well at the time of study, were negative. Family and close social contacts remained in good health and their stool specimens also tested negative.

Faecal specimens from four monkeys yielded *S. flexneri*, two being serotype 3 and two serotype Y. Faecal specimens yielding serotype 3 were re-tested by the Central Public Health Laboratory by the more reliable tube agglutination procedure using a heat-treated antigen suspension and correctly identified as serotype 1b (of identical type to that present in the human stool specimens). *Campylobacter jejuni* was also isolated from specimens of two monkeys. Stool specimens from the macaque with haemorrhagic colitis were negative for shigellae and other enteric pathogens.

DISCUSSION

Shigellae are non-motile Gram-negative bacilli. *S. flexneri* belonging to the B subgroup of the genus (the other subgroups being A, *dysenteriae*, C, *boydii* and D, *sonnei*). The B subgroup has nine major type antigens. The Y serotype identified in two of the monkeys is a group phase variant and can be derived from a number of major antigen serotypes (most frequently 4a). The 1b serotype, responsible for the three human cases reported here, was initially misclassified in specimens of two of the monkeys (for type 3) and is a known problem of the slide agglutination procedure of testing. The tube method, employing heat-treated antigen, is more reliable and confirmed the presence of a common serotype in both primate and human faecal specimens. Laboratory testing of specimens thereby supported the strong circumstantial evidence of occupationally acquired infection, employees having been in regular, direct contact with macaques harbouring an organism of common type and lacking other known risk factors.

Shigella flexneri causes a more severe illness than *S. sonnei* infection [10] which is the most common sub-type in the UK. [11]. Bloody diarrhoea and mucous discharge is often accompanied by abdominal pain, tenesmus, fever, anorexia, weight loss and dehydration. Toxic megacolon is a rare complication and may even occur when faecal culture is negative [12]. The illness has an appreciable mortality rate in the very young or debilitated.

Clinical illness may ensue from exposure to a low bacterial dosage – Ghosh reported an infective dose of 200 viable organisms in healthy volunteers [13], but more recent evidence favours an infective inoculum as low as 10 bacteria [14].

Infection occurs by the faeco-oral route, transmitted by food, water, fomites

and, possibly, flies [15]. The majority of cases in this country occur shortly after return from travel overseas; the incubation period is usually less than a week, though occasionally up to a month. For this reason, the history of travel in Turkey was excluded as a possible source of infection in one of the individuals involved in the outbreak. Faecal excretion of organisms after recovery from the acute illness may persist for a few weeks though usually ceases within a month.

In this outbreak, infection is likely to have occurred from direct contact with infected primate excrement, either as a result of a lapse in personal hygiene or inadvertent contamination of the face and mouth during aerosol-generating cleaning procedures, or a combination of both. The type of disposable respirator worn by employees would not have ensured adequate protection against infected aerosols. Alternatively, person-to-person spread may have occurred, e.g. via fomites.

Statutory quarantine procedures of imported primates are required by the Rabies (Importation of Dogs, Cats and other Mammals) Order 1974. Quarantine stations may perform routine stool-screening for enteric pathogens and commence antibiotic treatment but this does not guarantee that animals are free of infection on delivery to the primate house. Organisms may continue to be shed intermittently, commonly at times of stress, such as when animals are in transit [16].

Preventive strategies to reduce the risk of human infection require a combination of environmental controls, careful handling of animals and their excreta, maintenance of a very high standard of personal hygiene by those exposed and the wearing of appropriate protective clothing [17]. People working with primates should be aware of the risks involved and inform their doctors of the nature of their work when suffering from febrile symptoms or gastrointestinal complaints.

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