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One Health in Practice: A Pilot Project for Integrated Care of Zoonotic Infections in Immunocompromised Children and Their Pets in Chile

A. Peña[1,2], K. Abarca[1], T. Weitzel[3], J. Gallegos[4], J. Cerda[5], P. García[1] and J. López[6]

[1] Departamento de Enfermedades Infecciosas e Inmunología Pediátricas, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile
[2] Hospital Dr. Sótero del Río, Santiago, Chile
[3] Clínica Alemana de Santiago, Facultad de Medicina Clínica Alemana, Universidad del Desarrollo, Santiago, Chile
[4] Hospital San Javier, Linares, Chile
[5] División de Salud Pública y Medicina Familiar, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile
[6] Hospital Veterinario Puente Alto, Santiago, Chile

Impacts

- We present our experiences with a One Health pilot project of interdisciplinary management of zoonoses in immunocompromised children.
- The structured cooperation of medical and veterinary surgeons permitted to detect and treat zoonotic infections in immunocompromised children and their pets.
- Family-based information and visits, which aimed to improve pet management and prevent future zoonotic infection, were positively evaluated by all participants.

Keywords:
One Health; prevention & control; immunocompromised patient; pets; zoonoses

Correspondence:
A. Peña. Hospital Dr. Sótero del Río, Avenida Concha y Toro 3459, Santiago, Chile. Tel.: +56 225 764 626; Fax: +56 225 764 624; E-mail: anapena@med.puc.cl

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Summary

Although pets provide physiological and psychological benefits to their owners, they are a potential source of zoonotic infections, especially for vulnerable individuals such as immunocompromised patients. During 1 year, we therefore performed a pilot project, which included 32 immunocompromised Chilean children and their family pets (35 dogs and 9 cats) with the aim of detecting, treating and preventing zoonotic infections. Children were examined by Infectious Diseases paediatricians and demographical and clinical information related to zoonotic infections were recorded. Pets were examined and sampled by veterinarians, who also administered missing routine vaccines and anti-parasitics. During family visits, all members were informed and educated about zoonoses and a satisfaction survey was performed. Visits also included vector control and indoor residual spraying with pyrethroids. Children were re-examined and re-tested according to the findings of their pets, and all detected zoonotic infections were treated both in children and pets. Physical examination revealed abnormalities in 18 dogs (51.4%) and three cats (33.3%). Twenty-eight (63.6%) of the pets were diagnosed with a zoonotic pathogen, and seven (15.9%) with a facultative pathogen. Most zoonotic agents were isolated from the pet's external ear and intestine. Bacteria with the highest pathogenic potential were *Campylobacter jejuni* and *Brucella canis*. In two children and their respective pets, the same zoonotic diseases were diagnosed (toxocariasis and giardiasis). Arthropods serving as potential vectors of zoonotic infections were found in 49% of dogs and 44% of cats. The pilot project was positively evaluated by the participating families. Our pilot project confirmed that pets are reservoir for various zoonotic agents in Chile and that the implementation of an integrated multidisciplinary programme was a valuable tool to prevent, diagnose and treat such zoonotic infections in vulnerable patients such as immunocompromised children.

Introduction

Pets are important human companions providing physiological and psychological benefits to their owners. They encourage physical activity, relieve stress, and improve the overall quality of life, even controlling biological parameters such as blood pressure and heart rate (Friedmann and Son, 2009; Owen et al., 2010). These effects are especially beneficial for people with chronic diseases, and there are several animal-assisted therapy programmes (mainly using dogs) for patients with cancer during radiation or chemotherapy, HIV-infected individuals, persons with motor or mental disabilities as well as institutionalized older adults (Fleishman et al., 2015). Despite their positive influence on the well-being and health of their human owners, pets also bear the risk of zoonotic infections.

The situation in immunocompromised patients is more complex, as they are at higher risk of certain zoonotic diseases, which may cause more chronic or severe manifestation, depending on several factors such as age, disease type and stage, $CD4^{+}$ lymphocyte count, neutropenia and immunosuppressive therapy (Glaser et al., 2000; Hemsworth and Pizer, 2006; Mani and Maquire, 2009; Lamas et al., 2010; CDC, 2013). Opportunistic and/or dangerous pet-related pathogens include *Cryptosporidium*, *Bartonella*, *Salmonella*, *Campylobacter*, *Toxoplasma gondii*, *Toxocara* and microsporidia. It is recommended that pet-owning households with immunocompromised family members take special precautions to minimize the risk of zoonoses. These recommendations include the avoidance of exotic pet animals (such as reptiles, rodents and birds), sick or stray animals, and animals under 6 months of age, rigorous hygiene measures, adequate food for pets, and regular vector and parasite control (CDC, 2006; Tomblyn et al., 2009; López et al., 2013; NASPHV, 2013).

Over the last decades, approximately 75% of emerging human infectious diseases were classified as zoonotic (Taylor et al., 2001). Still, the prevalence of zoonoses in pet animals and their owners and the role of pets in transmitting these infections are unknown in most settings, as systematic studies are scarce. In Chile, a recent publication demonstrated the existence of several zoonotic agents in pets of immunocompromised children (Abarca et al., 2011) and other studies found emerging pet-associated pathogens in Chile including *Ehrlichia canis* and *Brucella canis* in dogs, *Bartonella henselae* in cats, and *Rickettsia felis* in cats fleas and dogs ticks (Ferrés et al., 2005; Abarca et al., 2007, 2013; Labruna et al., 2007; López et al., 2012). For social and cultural reasons, Chilean pet owners are prone to high-risk behaviours such as contact with animal saliva or faeces. To improve pet management and control the risk of zoonotic infections, a multidisciplinary approach including physicians and veterinarians seems beneficial, as advocated by the One Health initiative (One Health, 2009).

Here, we report our experience with an inter-disciplinary pilot project for the control and prevention of zoonoses in immunocompromised children living in households owning dogs or cats in Santiago, Chile.

Patients and Methods

The pilot project was performed between April 2013 and March 2014. From April to December 2013, we included children attending the Hematology & Oncology Unit of the Hospital Dr. Sótero del Río in Santiago, Chile. Inclusion criteria included immunocompromised state and/or immunosuppressive therapy, living in a household owning at least one pet dog or cat, and willingness to participate in the pilot project. After obtaining written consent from the patients and their parents, the children were evaluated by an Infectious Diseases paediatrician. This evaluation included demographical data, clinical history and information on pet ownership and care, as well as a physical examination. In parallel, the households of the respective children were visited by veterinarians three times. In the first visit, pets were examined for signs of diseases and for ectoparasites, samples were drawn, and demographical and clinical data as well as past use of vaccines and anti-parasitic drugs were recorded. On the second visit, pets received missing vaccines and, if necessary, systemic and/or topical anti-parasitic and other treatments, and family members were informed and educated. During a third visit, vector control was performed by indoor residual spraying with a pyrethroid; this procedure was repeated, if massive infestation was detected. A broad panel of laboratory exams was performed to detect various zoonotic pathogens using stool in patients, and stool, serum and skin samples in their pets (Table 1). All laboratory tests were performed at the microbiological laboratories of the Pontificia Universidad Católica and the Instituto de Salud Pública in Santiago, Chile. Depending on the clinical and laboratory findings of the respective pets, further examinations and treatments were performed. Clinical and laboratory evaluations of children were broadened in accordance with the zoonotic pathogens detected or suspected in the pets. Veterinary clinical and laboratory assessments were repeated in each episode of illness of pets during the study period. If zoonoses were diagnosed or suspected during follow-up visits, the respective child was also re-examined and re-tested according to the findings in its pet (*Toxocara canis* and *B. canis* serology, and *Campylobacter* stool culture). The affected pets were followed up by visits and phone calls until they were asymptomatic. All families were counselled about appropriate pet care, environmental hygiene, and zoonotic diseases using structured oral and written information for dogs and cats, which included appropriate choice of animal, nutrition, vaccination, use of anti-parasitics, and information on symptoms and signs of pets that need urgent veterinary care. At the end of the project, parents were asked to participate in a satisfaction survey. Furthermore, reports on the paediatric and veterinary results and findings were sent to the children's primary care physicians.

All medical costs related to the treatment of the patients were covered by their public health insurance, whereas all costs for the intervention in pets (veterinary controls, diagnostics, vaccines, and treatment) were financed by the study budget.

The study was approved by the Ethical Scientific Committee of the Servicio de Salud Metropolitano Sur Oriente, Santiago, Chile. Data analysis was performed using the descriptive statistical program Epi Info 3.4.1 (Centers for Disease Control and Prevention, Atlanta, GA, USA).

Table 1. Diagnostic protocol performed in 32 immunocompromised children and in their 44 pets

Subject	Sample	Diagnostic test	Agents to be detected
Children	Faecal	Routine O&P[a]	Intestinal parasites
	Faecal	Ziehl Neelsen modified stain	*Cryptosporidium* and other coccidians
Dogs	Faecal	Routine O&P[a]	Intestinal parasites
	Faecal	Ziehl Neelsen modified stain	*Cryptosporidium* and other coccidians
	Faecal	Stool culture	Bacterial enteropathogens
	External auditory canal swab	Aerobic culture	Bacteria and fungi
	Skin	Aerobic culture	Methicillin-resistant *Staphylococcus aureus* (MRSA)
	Serum	*Brucella canis* serology (IgG)[b]	*Brucella canis*
Cats	Faecal	Routine O&P[a]	Intestinal parasites
	Faecal	Ziehl Neelsen modified stain	*Cryptosporidium* and other coccidian
	Serum	Feline leukemia virus serology[c]	Feline leukemia virus
		Feline immunodeficiency virus serology[c]	Feline immunodeficiency virus
	Blood	Blood culture[d]	*Bartonella henselae*

[a]Burrows technique, three samples from different days were used.
[b]Immunofluorescence assay (Fuller Laboratories, Fullerton, CA, USA).
[c]Anigen rapid FIV Ab/FeLV Ag test kit (BioNote™, Inc., Gyeonggi-do, Korea).
[d]Lysis centrifugation technique, Isolator™ System (Wampole Labs, Princeton, NJ, USA).

Results

During the inclusion period of 9 months, 149 immunocompromised children attended the Hematology & Oncology Unit of the Hospital Dr. Sótero del Río in Santiago, Chile; 34 fulfilled the inclusion criteria and were invited to participate in the pilot project. Of those, 32 patients and their guardians agreed to participate; the 32 households included 35 dogs and nine cats. The median follow-up period was 8 months (range 3–12 months). As 12 children had more than one pet (2–4) and a pair of siblings shared one pet, there were a total of 45 child-pet pairs. Four of the households also owned one or more exotic pets (guinea pig, land hedgehog, parrot, rabbit, and hamster). The group of patients consisted of 17 girls and 15 boys with a median age of 9 years (range 1–18 years). Main causes of immunodeficiency were haematologic malignancies and solid tumours (leukaemia, 16; solid tumours, 11; osteopetrosis, 2; lymphoma, 1; cyclic neutropenia, 1; bone marrow aplasia, 1). Seventeen children were on chemotherapy and three were in palliative care; at enrolment, ten children were neutropenic and two had eosinophilia. Two children had a history of a zoonotic infection (toxocariasis). Stool examinations for intestinal parasites detected *Giardia intestinalis* cysts in one symptomatic child with diarrhoea and apathogenic protozoa in two asymptomatic children (*Entamoeba coli*, *Blastocystis hominis*).

The examined 35 pet dogs had a median age of 4 years (range 2 months to 12 years); two dogs were puppets <6 months of age. Only five dogs were completely immunized and none had received regular anti-parasitic treatment. Eighteen (51.4%) showed abnormal clinical findings, 17 (47%) harboured ectoparasites and 8 (21.6%) endoparasites, and in 12 (32.4%) bacterial or fungal microorganisms were isolated (Table 2). The nine cats had a median age of 1 year (range 4 months to 5 years), and two were <6 months of age. None had complete immunizations, and only one had received anti-parasitic drugs. Three (33.3%) showed abnormal clinical findings, four (44.4%) harboured ectoparasites. Six (67.7%) had endoparasites, and four (44.4%) had positive cultures for bacterial or fungal microorganisms (Table 2). In total, 28 (63.6%) pets were diagnosed with a zoonotic pathogen, and seven (15.9%) with a facultative pathogen. A variety of bacteria were isolated, mainly from symptomatic pets with ear infections. Still, bacteria with the highest pathogenic potential were detected by stool culture (*Campylobacter jejuni*) and by serology (*B. canis*). Cultures for resistant *Staphylococcus aureus* strains (MRSA) were all negative, as were blood cultures for *Bartonella*. Various parasites were diagnosed, some with a relevant potential of zoonotic infections, such as *Toxocara* spp., *Sarcoptes scabiei* and *G. intestinalis*. Only one fungal microorganism (*Aspergillus terreus*) was detected. One cat had feline immunodeficiency virus infection and was vaccinated; the animal presented with diarrhoea at admission and later developed an ear abscess. None of the pets harbouring a zoonotic agent died or was euthanized and all remained at their respective homes. All bacterial and mycotic infections were treated with antimicrobials; after treatment, all pets were asymptomatic.

Two patients and their respective pets (4.4%) were affected by the same zoonotic infection. The first patient was diagnosed with toxocariasis by serology and lived with a dog, which had active *T. canis* infection. The second suffered symptomatic giardiasis and had a dog, which shed *Giardia* cysts.

Of 31 parents, 22 (70.9%) responded to the satisfaction survey. All found the intervention useful and beneficial to their child's health, 85% felt that it helped to improve their pet's health care, and 60% found that it helped to change inappropriate animal care customs.

The average cost per pet spent for veterinary controls, diagnostics, vaccines and treatment was 330 US$.

Discussion

The benefits obtained by contact with pets are multiple (physical and psychological) (Friedmann and Son, 2009; Owen et al., 2010), especially for chronically ill patients and also those with immunodeficiencies, who are at an increased risk of dangerous and difficult to treat zoonotic infections (Hemsworth and Pizer, 2006; Mani and Maquire, 2009; Lamas et al., 2010; CDC, 2013). As a recent study in pet owners in Canada showed, high-risk exposure such as scratches and bites are frequent and most pet owners never receive information regarding pet-associated disease risks (Stull et al., 2012). Similar findings were reported from Chilean households with immunocompromised children (Abarca et al., 2011). These findings highlight the importance of an adequate management and prevention of zoonotic diseases especially for individuals at high risk. The lack of structured cooperation between human and animal health disciplines has led to the 'One Health' initiative, which breaks up with some of the traditional viewpoints of human and animal health and promotes inter-disciplinary approaches to control zoonotic diseases (American Veterinary Medical Association, 2008; One Health Commission, 2009). For our project, we therefore used a multidisciplinary team of medical and veterinary surgeons and nurses to optimize the management and prevention on zoonoses in the participants and their pets.

Our results confirmed that our patient's pet dogs and cats represent a reservoir of potentially severe zoonotic infections. Furthermore, we found that most of the included pets had not received routinely recommended vaccines and anti-parasitics. Various microorganisms including bacteria, endoparasites and ectoparasites, and fungi were detected in 70.5% of the examined pets, many of them zoonotic pathogens or vectors of zoonotic infections. As many relevant pathogens such as *Staphylococcus intermedius* and *Streptococcus canis* were isolated from cultures of pets with signs of external ear infections, regular ear examinations are highly recommendable.

Table 2. Clinical conditions, parasites and microorganisms detected in 44 pets of households with immunocompromised children

Clinical and microbiological findings	Location	Dogs (n = 35)	Cats (n = 9)
Clinical diagnosis			
Periodontal disease		6	1
Dermatitis		5	–
Otitis		4	4
Conjunctivitis		2	–
Sarcoptic mange		1	–
Demodicosis		1	–
Tracheobronchitis		–	4
Other		9	–
Ectoparasites			
Rhipicephalus sanguineus[a]	Skin	7	–
Ctenocephalides spp.[a]	Skin	11	4
Sarcoptes scabiei[a]	Skin	1	–
Demodex canis	Ear	1	–
Otodectes cynotis	Ear	–	1
Protozoa			
Giardia intestinalis[a]	Intestinal	3	3
Helminths			
Trichuris vulpis	Intestinal	4	–
Toxocara canis[a]	Intestinal	1	–
Toxocara cati[a]	Intestinal	–	1
Toxascaris leonina[a]	Intestinal	–	1
Dipylidium caninum[a]	Intestinal	–	1
Bacteria			
Campylobacter jejuni[a]	Intestinal	3	–
Brucella canis[a]	Serum	5	–
Staphylococcus intermedius[a]	Conjunctiva	2	–
	Ear	3	–
	Uterus	1	–
Streptococcus canis[a]	Ear	1	–
Escherichia coli[b]	Ear	–	1
Acinetobacter spp.[b]	Ear	–	1
Staphylococcus spp. (coagulase-neg.)[b]	Ear	1	–
Corynebacterium spp.[b]	Ear	1	–
Bacillus spp.[b]	Ear	–	1
Fungi			
Aspergillus terreus[b]	Ear	–	1
Viruses			
Feline immunodeficiency virus	Serum	–	1

[a]Zoonotic pathogen or vector.
[b]Zoonotic facultative pathogen.

Staphylococcus intermedius is an emerging human zoonotic pathogen, which was isolated in 17% of examined dogs. It is a normal inhabitant of canine skin and oral cavity and may cause serious infections in humans such as bacteremia, pneumonia, arthritis, cerebral and skin abscesses after transmission by bites or by direct contact (Wang et al., 2013). It might be underdiagnosed as misidentifications as *S. aureus* are common (Pottumarthy et al., 2004). *Streptococcus canis* is a betahaemolytic streptococcus of the Lancefield group G, which has been associated with human skin infections and endocarditis and which might be also underdiagnosed due to its difficult identification (Lam et al., 2007; Lacave et al., 2015).

Intestinal carriage of *C. jejuni* was found in three asymptomatic dogs. The respective children were tested by stool culture, but were *Campylobacter* negative. The three pets were treated with anti-microbial to avoid the risk of transmission. *Campylobacter* is a common zoonotic pathogen and might also be transmitted through pet contact. In a recent study, these bacteria were isolated in 21% and 29% of diarrhoeic cats and dogs, respectively, more frequently in animals younger than 1 year, and in 4% of asymptomatic pets (Holmberg et al., 2015). The disease is usually self-limited; however, in immunocompromised patients, infections might be chronic and disseminated (Wolfs et al., 2001; González-Abad and Alonso-Sanz, 2013).

Brucella canis was diagnosed by serology in four asymptomatic dogs and one dog with orchitis, which is in accordance with previous epidemiological data from Chile (Troncoso et al., 2013). The dogs were pets of three children, who were all without clinical signs of brucellosis and negative by *B. canis* serology. Preventive anti-microbial therapy was administered to the dogs, and they were sterilized to reduce the risk of chronic infection and transmission to their owners and other dogs. In humans, *B. canis* can cause prolonged fever, endocarditis, osteoarticular infections and bacteremia. Its incidence in immunocompromised patients is unknown, but infections in HIV-infected patients have been described (Lucero et al., 2010; Lawaczeck et al., 2011).

Pets are a known reservoir for multiresistant bacteria such as MRSA and ESBL- or carbapenemase-producing enterobacteria (Rankin et al., 2005; Rutland et al., 2009; Schmiedel et al., 2014; Woodford et al., 2014). In our project, however, no strains of MRSA or other multiresistant bacteria were isolated.

One cat suffered from feline immunodeficiency virus infection. The animal presented diarrhoea at admission and subsequently developed an ear abscess. This lentivirus does not infect humans, but it increases the risk of secondary infections by various zoonotic agents such as mycoplasmas, mycobacteria and dermatophytes (Sellon and Hartmann, 2008). Feline leukaemia virus is a retrovirus that also increases the risk of zoonotic infections especially with *B. henselae* (Hartmann, 2008; Buchmann et al., 2010). The absence of feline leukaemia virus in cats of our patients probably explains that *B. henselae* was not detected in any of the feline blood cultures.

In pet dogs and cats, intestinal protozoa such as *G. intestinalis* and cryptosporidia can cause a wide spectrum of clinical symptoms from subclinical to abdominal pain and diarrhoea (López et al., 2006; Tysnes et al., 2014). Both are important human pathogens, although the epidemiological role of zoonotic transmission of giardiasis is still under investigation (Ryan and Caccio, 2013). In patients with cellular immunosuppression, cryptosporidia cause severe opportunistic infections with chronic diarrhoea and weight loss (wasting syndrome; CDC, 2013). Despite the low rate of intestinal protozoa found in our patients, the case of giardiasis in a child/pet pair highlights the importance of veterinary controls of diarrhoeic and very young pets to avoid faecal–oral transmission of such pathogens.

Only few pets harboured human-pathogenic helminths. Most importantly, one dog and one cat were carriers of *Toxocara*, a frequent cause of pet-associated human zoonoses. In Chile, the prevalence of this parasite is high in animals and in asymptomatic humans (López et al., 2006; Weitzel et al., 2013). The fact that the patient living with the dog infected with *T. canis* had a positive *Toxocara* serology indicates the importance of regular deworming to prevent transmission of this parasite.

Vectors were found in almost half of the examined dogs and cats. These arthropods are known vectors of rickettsial pathogens, which have recently been described in Chile (Abarca et al., 2007, 2013; Labruna et al., 2007; López et al., 2012).

Four of the households also owned exotic pets such us poultry, rodents and reptiles. These animals are important reservoirs for various microorganisms including *Salmonella*, *Yersinia*, *Cryptococcus*, *Histoplasma*, *Mycobacterium avium*, *Chlamydia psittaci*, lymphocytic choriomeningitis virus and cryptosporidia, and should therefore be avoided in families of immunocompromised patients (Hemsworth and Pizer, 2006; Greene and Levy, 2008; Mani and Maquire, 2009).

Our study demonstrated the spectrum of potential exposure to zoonotic agents in our patients. Still, case–control studies are necessary to estimate the exact transmission risk. Although the costs of surveillance and care of zoonoses in pets were relatively low, they might have been too high for many Chilean families with low income. Pet-related costs are not covered by public health insurances. Therefore, financial issues could be a relevant obstacle to implement structured pet health programmes for immunocompromised pet owners in low- or middle-income countries.

In conclusion, our pilot project followed a One Health approach by implementing an inter-disciplinary care for immunocompromised patients including their families, who live with pets. Our data confirmed that pets are an important reservoir for various zoonotic agents in Chile. The structured cooperation of medical and veterinary surgeons permitted to detect and treat zoonotic infections in immunocompromised children and their pets and allowed the immunocompromised patients to keep their pets in their homes and enjoy their benefits. Furthermore, it helped to provide education and counselling on zoonoses, which was highly valued by the participating families. We believe that the experiences of our pilot project provide important information on how to implement future One Health programs of integrated care in Chile and other countries.

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Conflict of Interest

The authors declare that they have no conflict of interests.

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