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A One-Health integrated approach to control fascioliasis in the Cajamarca valley of Peru

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Abstract. *Fasciola hepatica* infection is reported from many Latin American countries, with very high prevalence rates in both humans and livestock in the Andean countries. Due to its environmental characteristics, particularly suitable for liver fluke infection, the Cajamarca valley of Peru has often been chosen as a model to study the epidemiology of liver fluke infection in the Andes. In this paper we describe the profile of a project aimed at a multidisciplinary and integrated approach for the control of fascioliasis in animals and humans in this valley. The One-Health integrated approach applied here is based on accurate and sensitive diagnostics, namely the FLOTAC, and the use of geospatial tools for epidemiological scrutiny.

Keywords: *Fasciola hepatica*, FLOTAC, geographical information systems, One-Health, Cajamarca, Peru.

Introduction

Fasciola hepatica and *F. gigantica* are the two trematodes, which cause human and animal fascioliasis (fasciolosis). These parasites are liver flukes with a wide host range (e.g. sheep, cattle and water buffaloes) and wild animals (e.g. rabbits, beavers, deer and rats) (Robinson and Dalton, 2009). These parasites are well known owing to their worldwide veterinary importance and negative economic impact on livestock production (Robinson and Dalton, 2009). Human infections have been reported from 51 countries in five continents (Mas-Coma et al., 2009). Recent estimates suggest that more than 90 million people are at risk of fascioliasis with 2.4 to 17 million individuals infected (Keiser and Utzinger, 2009). The recent emergence of *F. hepatica* infection all over the world, as well as the long-term pathogenicity caused, prompted the World Health Organization (WHO) to include human fascioliasis on its list of priorities among the neglected tropical diseases (NTDs) (WHO, 2008; reviewed in Mera y Sierra et al., 2011).

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In the Americas, fascioliasis is exclusively caused by *F. hepatica* (Mas-Coma et al., 2009), mainly transmitted by lymnaeid snail intermediate hosts of the *Galba/Fossaria* group (Bargues et al., 2007). Very high prevalence rates of *F. hepatica* infection have been reported from many Latin American countries, both in humans and livestock, particularly in the Andean countries at high and very high altitudes where transmission appears to be enhanced as a consequence of the adaptation of both parasite and its intermediate snail host to the extreme environment in these mountains (Mas-Coma et al., 2001). In the Andean countries of South America, fascioliasis is therefore a serious "One-Health" problem, both from the veterinary and the human public health point of view. Among these high-altitude countries, Peru appears to present a comparatively large human fascioliasis health problem (González et al., 2011). Indeed, there is a high prevalence of fascioliasis in the Peruvian highlands, but most human cases remain undiagnosed. A recent study performed by Lopez et al. (2012) in Cusco showed that subclinical fascioliasis was common among children and strongly associated with anaemia. The Cajamarca valley of Peru has often been chosen as a model for the study of the epidemiology of liver fluke infection in the Andes (Fuentes, 2006). This is due to its environmental characteristics, which are particularly suitable for *F. hepatica* transmission (Fig. 1). As recently reviewed by González et al. (2011), the fasci-

Fig. 1. Views of the study area, the Cajamarca valley of Peru, showing environmental characteristics particularly suitable for liver fluke infections.

oliasis problem in Cajamarca appears early on in the literature and has therefore attracted many multidisciplinary studies on different aspects of *F. hepatica*, however mostly related to human infections (e.g. Ortiz et al., 2000; Espinoza et al., 2007; González et al., 2011; Valero et al., 2012). Some authors have recently reported very high overall *F. hepatica* prevalence rates (24.4%) with the highest rate (47.7%) found in local human populations (González et al., 2011), demonstrating that Cajamarca province is a hyperendemic area for human infection according to the WHO epidemiological classification (Mas-Coma et al., 2001, 2009; Mas-Coma, 2005).

Due to the importance of fascioliasis in the Cajamarca valley of Peru, the project "Control integrado de la Distomatosis Hepática en la Región: Cajamarca, Cajabamba, San Marcos, Celendín, San Pablo, San Miguel" promoted by FONCREAGRO (El Fondo de Crédito para el Desarrollo Agroforestal) started in 2011 and is currently ongoing. Geospatial tools (for territorial sampling, mapping, climate-based forecasting and surveillance), together with new sensitive diagnostic techniques, the FLOTAC techniques (Cringoli et al., 2010), have been selected to form the basis of the project (see flowchart in Fig. 2) that is aimed at a multidisciplinary and integrated approach for the control of fascioliasis in animals and humans in the Cajamarca valley of Peru.

The project

After staff selection and hiring, the construction, set-up of the diagnostic laboratory and the training of personnel on diagnosis and geospatial tools took place during the biennium 2010-2011. The project started with the planning of field activities as the first step, i.e. a geographical information system (GIS) study of the area using Arc-GIS 9.2 GIS software (ESRI, Redlands, CA, USA). The GIS was constructed utilizing the administrative boundaries (at province and district levels) of the study area. The study area, located in the northern highlands of Peru between latitudes 78°48'31"N and 6°40'20"S and longitudes 77°56'49" N and 7°45'35"S, includes six provinces (Cajamarca, Cajabamba, San Marcos, Celendín, San Pablo and San Miguel) and 17 districts (Fig. 3) and

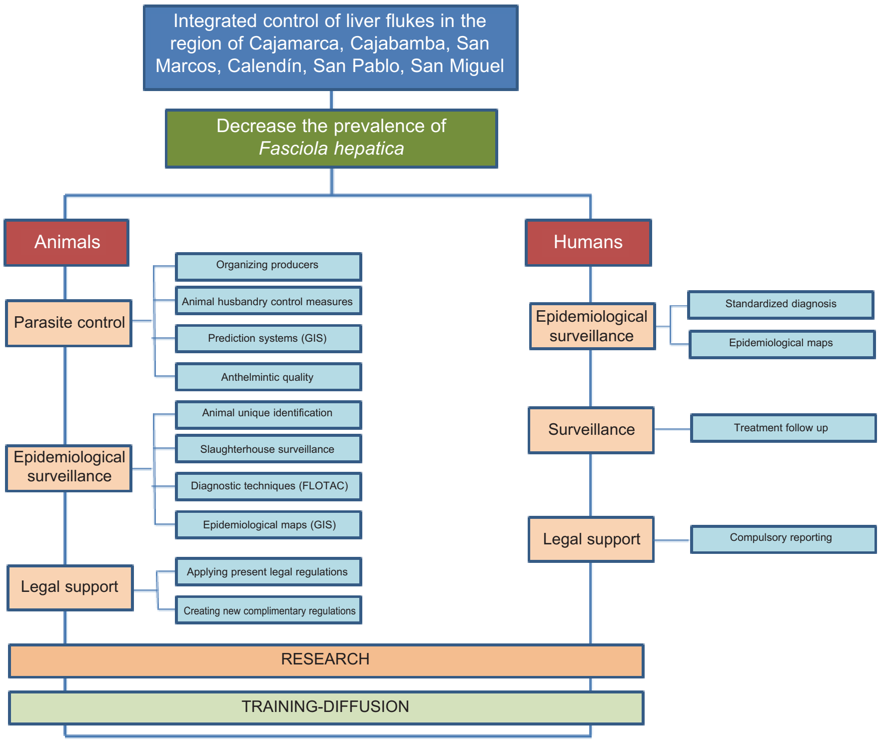

Fig. 2. Scheme of the proposed "One-Health" integrated approach to control fascioliasis in the Cajamarca valley of Peru.

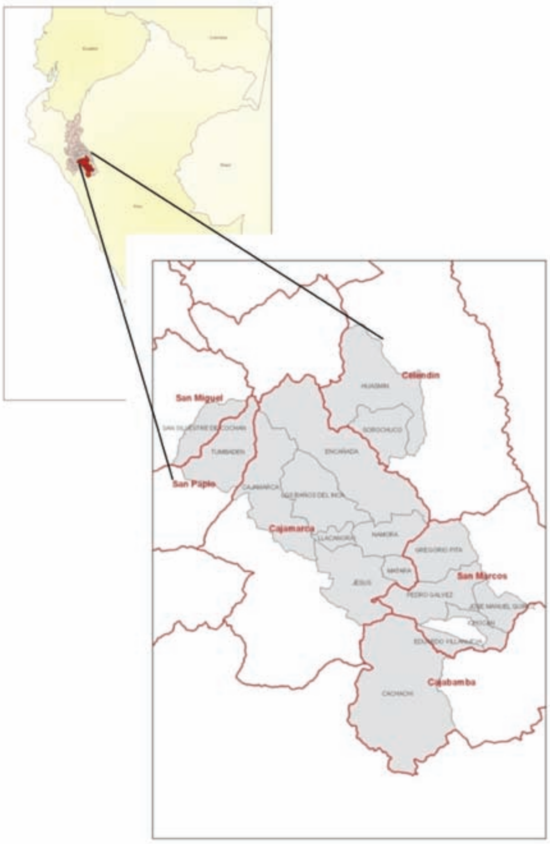

Fig. 3. The study area, the Cajamarca Valley of Peru.

extends from 1,990 to 3,256 m above the mean sea level (MSL). The climate is equatorial (mild, dry and sunny), which creates very fertile soil. In the study area, the rural population is 31,256s, whereas the number of cattle is 158,419. The maps (Fig. 4 a,b) report the rural population and bovine population in the study area, stratified according to the provinces and districts. The *caseríos* (hamlets, small villages), i.e. the smallest political division in Peru, were selected as the epidemiological units of this project (Fig. 5). In each *caserío*, there are a certain number of small producers with an average of 100 families, each family (or producer) owning 8 to 10 cattle. For project purposes, all the *caseríos* (n = 710) of the region were geo-referenced (Fig. 6a) and integrated into the GIS database.

Baseline *F. hepatica* prevalence data will be collected from 183 *caseríos*. This sample size was calculated using the formula proposed by Thrusfield (1995) with the following assumptions: study population = 710 *caseríos*, expected prevalence of *F. hepatica* in cattle = 80% (based on literature data), confidence interval = 95%, and desired absolute precision = 5%.

In order to uniformly sample the 183 *caseríos* throughout the entire region, a 10 × 10 km grid was overlaid on the region map within the previously

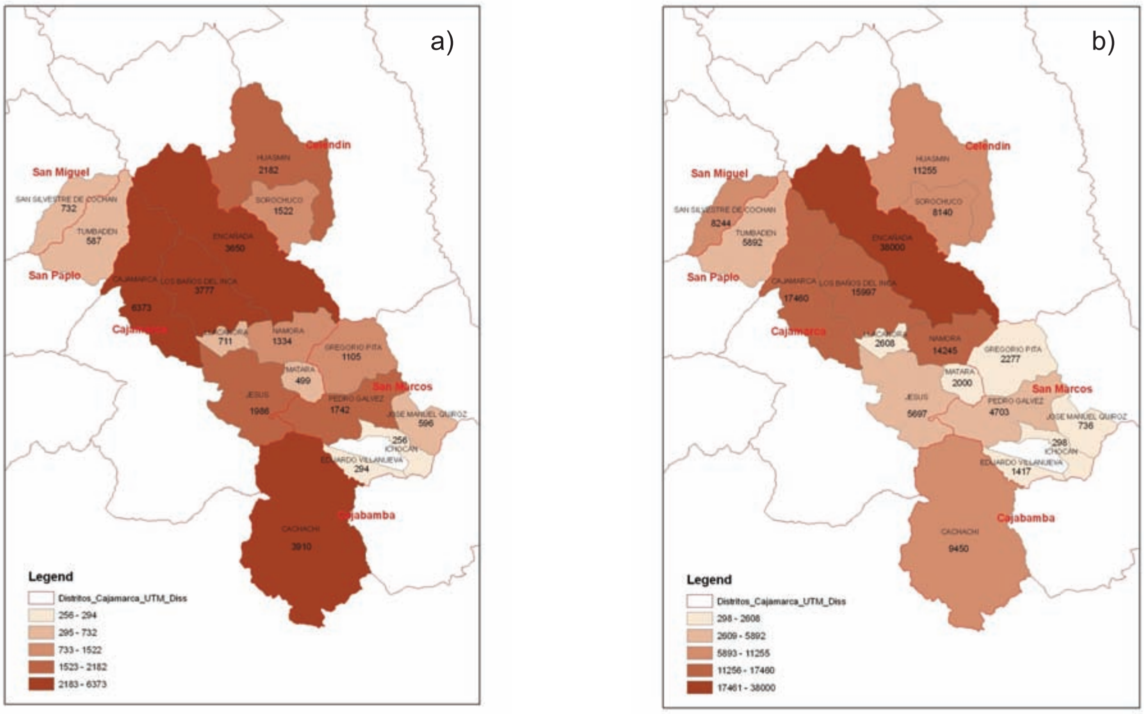

Fig. 4. The study area; rural population (a) and bovine population (b), stratified according to the provinces and districts.

established GIS. As a result, the territory of the region was divided into 70 equal quadrants (Fig. 6b). During the baseline survey, a number of *caseríos* proportional to the number of *caseríos* in the quadrant (at least one *caserío* per quadrant) will be randomly selected among those present in the GIS database (Rinaldi et al., 2006). Thus, 10 families were randomly selected in each *caserío* and for each family two adult cattle sampled to make up a total of 20 samples per *caserío*.

Once at the laboratory, pooled samples of the two cattle will be prepared and analysed using the FLOTAC double technique with a zinc sulphate-based flotation solution (FS7, density = 1.35; in Cringoli et al., 2010). Overall, 10 FLOTAC analyses will be performed per each *caserío* for a total of 1,830 copromicroscopic examinations.

After obtaining the baseline prevalence data for the 183 *caseríos,* we will proceed with the treatment of all the cattle in all the 710 geo-referenced *caseríos* of the study area utilizing clorsulon in combinantion with ivermectin. These drugs were chosen due to the fact that recent reports from Rojas Moncada (2007, 2012) and Ortiz (2012) have indicated the development of *F. hepatica* resistance against triclabendazole and closantel. In the studies performed by Rojas Moncada (2012) the author reports that the only two molecules still active against Cajamarca isolates of *F. hepatica* are clorsulon and nitroxinil.

Fig. 5. Examples of *caseríos*, the epidemiological units of the project.

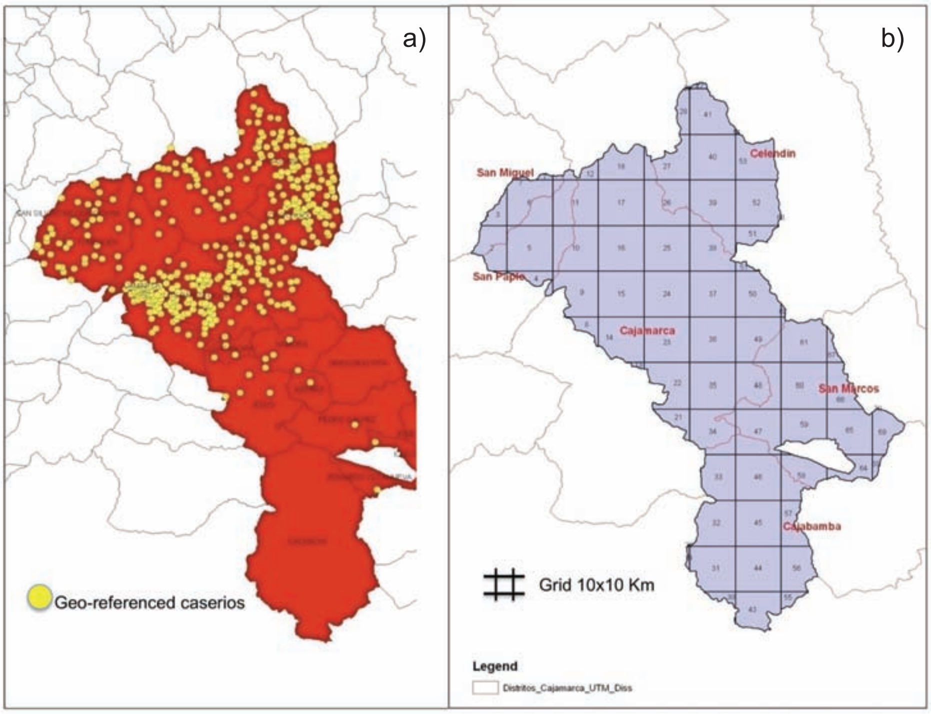

Fig. 6. Geo-referenced *caseríos* (a) and grid (10 x 10 Km) overlayed on the study area (b) for sampling.

Discussion

There is a need for accurate and sensitive epidemiological and diagnostic tools, so that the true extent and global burden of fascioliasis in animals and humans can be estimated and the impact of interventions quantified and monitored (Keiser and Utzinger, 2009). In this paper we describe an ongoing interdisciplinary project to control fascioliasis in the Cajamarca valley of Peru based on a "One-Health" integrated approach, using the FLOTAC techniques (Cringoli et al., 2010) and GIS (Rinaldi et al., 2006) as novel diagnostic and epidemiological tools.

Regarding diagnosis, it should be noted that egg detection in faecal samples is the most common approach for the diagnosis of *F. hepatica* infection in humans and animals, methods including Kato-Katz thick smear, formalin-ethyl-acetate technique, Stoll's dilution egg count method, sedimentation techniques, and flotation-based techniques (e.g. McMaster) (Cringoli et al., 2010; Fürst et al., 2012). FLOTAC has been suggested as the method of choice to diagnose infections with *F. hepatica* in animals and humans (e.g. Duthaler et al., 2010)

Concerning the epidemiology, *F. hepatica* infection is an outcome of multiple determinants and geospatial tools can answer questions about the complex web of causation of epidemiological patterns of infections. Furthermore the importance of these tools is due to the fact that the challenge for gaining large-scale control of fascioliasis cannot be addressed without considering both abiotic and biotic environmental factors that affect the maintenance and transmission of the parasite. The pioneering studies by Malone et al. (1992, 1998) formed the basis of the application of satellite surveillance and GIS for studies on *F. hepatica* (Malone et al., 2001). Indeed, due to the life cycle of *F. hepatica*, which involves amphibious snails as intermediate hosts, and thus has strong environmental determinants and strong needs of water, geospatial models of infection risk are nowadays becoming increasingly sophisticated and precise, with more refined data analysis programmes and GIS data (Fairweather, 2011). Fascioliasis exhibits an exceptionally large latitudinal, longitudinal and altitudinal distribution (Mas Coma et al., 2009). For these reasons, the application of geospatial tools such as GIS, global positioning systems (GPS), satellite-based remote sensing and virtual globes (e.g. Google Earth™) (Utzinger et al., 2011) to spatial epidemiology of *F. hepatica* infection have been firmly established for mapping, forecasting, monitoring, early warning and surveillance. *F. hepatica* is a good candidate for geospatial tools owing to its environmental sensitivity, tendency to year-to-year geographic stability in snail host habitat distribution, relative longevity in mammalian hosts and confinement of livestock in identifiable grazing areas. The critical factors for *F. hepatica* development are temperature and humidity and the normalized difference vegetation index obtained from remote sensing is associated with suitable moisture availability to external stages of liver fluke; the combination of management factors with characterization of snail habitats is a powerful means to predict the infection risk with *F. hepatica* in a given region (Charlier et al., 2011).

In conclusion, the geospatial-based "One Health" approach proposed in the project could be necessary for efficient management and control of *F. hepatica* in Peru, Latin America and beyond.

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