Semina: Ciências Agrárias
ISSN: 1676-546X
semina.agrarias@uel.br
Universidade Estadual de Londrina
Brasil

Aleixo, Marcos André; França Freitas, Deivid; Hermes Dutra, Leonardo; Malone, John;
Freire Martins, Isabella Vilhena; Beltrão Molento, Marcelo
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Semina: Ciências Agrárias, vol. 36, núm. 3, mayo-junio, 2015, pp. 1451-1465
Universidade Estadual de Londrina
Londrina, Brasil

DOI: 10.5433/1679-0359.2015v36n3p1451

Fasciola hepatica: epidemiology, perspectives in the diagnostic and the use of geoprocessing systems for prevalence studies

Fasciola hepatica: epidemiologia, perspectivas no diagnóstico e estudo de prevalência com uso de programas de geoprocessamento

Marcos André Aleixo[1]; Deivid França Freitas[2]; Leonardo Hermes Dutra[1]; John Malone[3]; Isabella Vilhena Freire Martins[4]; Marcelo Beltrão Molento[1,5*]

Abstract

Fasciola hepatica is a parasite that is located in the liver of ruminants with the possibility to infect horses, pigs and humans. The parasite belongs to the Trematoda class, and it is the agent causing the disease called fasciolosis. This disease occurs mainly in temperate regions where climate favors the development of the organism. These conditions must facilitate the development of the intermediate host, the snail of the genus *Lymnaea*. The infection in domestic animals can lead to decrease in production and control is made by using triclabendazole. Triclabendazole resistance in *F. hepatica* has been reported worldwide including in Brazil. Another concern is the increase number of human cases with the consumption of contaminated vegetables in regions where sanitation is inadequate together with the presence of infected animals and the absence of efficient control methods. The knowledge of the epidemiology of animal fasciolosis, including their occurrence, distribution and monitoring with techniques such as PCR and ELISA is reaching a new level with the usage of the Geographic Information System. The objective is to use new technologies for early fasciolosis diagnostic, as well as, to develop geoprocessing technics that could allow the determination of its prevalence and the evolution of clinical cases in animals before hand. This review paper provides an overview of *F. hepatica*, covering the aspects listed above, including original data.
Key words: *Fasciola hepatica*, epidemiology, geographic information system, zoonosis

Resumo

Fasciola hepatica é um parasita que se localiza no fígado de ruminantes, podendo infectar equinos, suínos e humanos. O parasito pertence à classe Trematoda, sendo o agente responsável pela doença denominada fasciolose, que ocorre principalmente em regiões temperadas, com clima favorável para o desenvolvimento do organismo. Tais condições devem auxiliar no desenvolvimento do hospedeiro intermediário, o molusco do gênero *Lymnaea*. Existe uma crescente preocupação quanto ao número de casos humanos diagnosticados em certas regiões cujo saneamento básico é inadequado, há presença de animais infectados e cultura em consumir hortaliças de áreas contaminadas cruas ou pouco cozidas.

1 Discentes de Doutorado, Laboratório de Doenças Parasitárias, Deptº de Medicina Veterinária, Universidade Federal do Paraná, UFPR, Curitiba, PR. Brasil. E-mail: marcos.aleixo@cescage.edu.br; leonardodutra@hotmail.com
2 Discente de Doutorado, Programa de Pós Graduação em Biociências e Biotecnologia, Universidade Estadual do Norte Fluminense Darcy Ribeiro, UENF, Campos dos Goytacazes, Brasil. E-mail: dfnaweb@hotmail.com
3 Prof., Department of Pathobiological Sciences, Lousiana State University, Baton Rouge, LA, USA. E-mail: malone@vetmed.lsu.edu
4 Profª, Programa de Pós Graduação em Ciências Veterinárias, Universidade Federal do Espírito Santo, UFES, Alegre, Brasil. E-mail: dfnaweb@hotmail.com
5 Pesquisador, National Institute of Science and Technology, INCT-Pecuária, Belo Horizonte, MG, Brasil. E-mail: molento@ufpr.br
* Author for correspondence

Recebido para publicação 02/11/13 Aprovado em 17/03/15

O parasitismo em animais domésticos pode levar a uma queda no desempenho animal e seu controle é realizado, principalmente, com o uso do triclabendazole. Entretanto, relatos quanto à resistência do patógeno à este produto vêm sendo descritos, inclusive no Brasil. O conhecimento da epidemiologia da fasciolose animal, incluindo sua ocorrência, distribuição e monitoramento com técnicas laboratoriais como o ELISA e a PCR, estão tendo um novo progresso com a utilização do Sistema de Informação Geográfica. O objetivo de utilizar essas novas tecnologias é diagnosticar a fasciolose mais precocemente, assim como, desenvolver técnicas de geoprocessamento que possam determinar a prevalência e a evolução dos casos em animais. Este artigo aborda recentes avanços no monitoramento da *F. hepatica*, cobrindo alguns aspectos listados acima, compilando dados inéditos.
Palavras-chave: *Fasciola hepatica*, epidemiologia, diagnóstico, zoonose

Introduction

Epidemiology of the disease

Fasciolosis is a disease caused by the trematode *Fasciola hepatica* that was described predominantly in temperate climate regions worldwide. *Fasciola hepatica* is the only species found in Brazil, while *F. gigantica* is located in the tropics of Africa and Asia. There is an overlap in their distribution in the Central Asia and East African regions, where hybrid forms of the parasite have been isolated (MAS-COMA, 2005). The adult form of the parasite measures between 20 to 50 mm long and 6 to 12 mm wide, inhabiting the bile ducts of various kinds of hosts, such as ruminants, horses, rabbits, hares, rats, including humans (TAYLOR; COOP; WALL, 2007). Thus, the success of *F. hepatica* as a parasite depends on its ability to infect and complete its cycle in a wide range of mammalian hosts.

The occurrence of the disease is fundamentally linked to the mollusk of the gender Lymnaea sp. presence, which acts as the agent's intermediate host, eliminating the infective stage of cercaria (MAS-COMA, 2005). In addition to this, the temperature between 10 to 25°C, the low elevation areas, the hydrography with the presence of flooded and wetlands areas, the irrigated rice cultivation and the extensive livestock breeding are factors that contribute to the maintenance of the mollusk and to the spread of fascioliasis (ANDREWS, 1999). These are important factors for the development of large amounts of metacercariae, which would configure high infection rates (TAYLOR; COOP; WALL, 2007). Bowman (1995) emphasized that even after a dry season, some places are still partially wet, supporting animal grazing. In these places, the metacercariae can keep their viability with its consequent passive ingestion and disease development.

However, in certain places the temperature by itself is not the most important factor for the transmission and maintenance of fasciolosis. Tum, Puotinen and Copeman (2004) observed in Cambodia that even though the rivers that cross the country were mostly coming from the melting snow in the highest mountains, which gave some stability to these bodies of water throughout the year, many of these areas were constantly flooded due to occasional rain, turning these places into ideal areas for the transmission between the parasite and its intermediate and definitive hosts. In countries such as Chile, the United States, Ireland and Egypt, endemic fascioliasis has been associated with low altitude regions, in view of the other unfavorable factors that can be found in high altitude regions, imposing a higher soil evaporation rate and lower temperatures. Thus, pastures or urban areas in high peak places are more difficult to have accumulating water and the formation of wetlands, which could consequently reduce the lifespan of the intermediate host.

In southern Brazil, the cities that are up to approximately 150 m above the sea, had higher levels of infected cattle with *F. hepatica*, demonstrating that the altitude factor was important to the development of the disease (DUTRA et al., 2010). However, Dalton (1999) determined hyper-endemic fasciolosis areas in high altitude regions (1.500m above sea level) in Peru. Mas-Coma, Funatsu and Bargues (2001) reported that in places of high altitude where the *F. hepatica* is present, some factors might ensure the spread of disease in cattle and in humans. In their studies in higher altitudes (3.800m above sea level) in Bolivia, they observed that the proximity to the Equator guarantee the temperature increase and therefore the moisture due to high evaporation. The existence of bodies of water in that place was due to the melting of the Andean mountain, which, combined with the existence of shallow water tables in the soil from the Titicaca Lake, ensured the permanent collections of freshwater.

Economic Impact

Fasciolosis has a great impact on the world's economy, due to its high incidence, directly affecting animal production (MAS-COMA, 2005). The high prevalence of fasciolosis in cattle was reported in all continents and is a serious problem in countries like Chile (94%), the United States (52.7% – Florida 68%), Ireland (45%), Spain (29.5%), Turkey (29.3%), Peru (29%), Germany (10.7%), Morocco (10.4%), Cambodia (10%) and New Zealand (8.5%) (TUM et al., 2007; TORGERSON; CLAXTON, 1999). In Brazil, Klimionte et al. (2005) revealed that cities such as Boa Vista do Incra, Maquiné and Presidente Lucena from the state of Rio Grande do Sul, had an incidence of 68, 84, and 91%, respectively. Gomes et al. (2002) found an infection rate of 15.38% in cattle slaughtered in Campos dos Goytacazes, Rio de Janeiro State. The same authors found an infection rate of 5.22% by pedogenetic forms of *F. hepatica* in *L. columella* in a farm located in the same city.

As seen above, *F. hepatica* has a wide distribution in Brazil and according to last-decade data for the average of parasites found in bovine liver from all the Brazilian states under the Database of the System of Management Information of the Federal Inspection Service of the Ministry of Agriculture (SIGSIF/MAPA), Rio Grande do Sul and Santa Catarina had prevalence rates of 18.6 and10.1%, respectively between 2003-2008 (Figure 1), followed by Rio de Janeiro and Paraná. Bernardo et al. (2011) found a prevalence of 24.9% between 2006 and 2009 in Espírito Santo according to the SIGSIF/MAPA (Figure 1). The present Map reflects the most updated information about the distribution of the disease and may be used for important animal health decision-making at the Federal and State level.

The economical impact is more significant when animals show prevalence above 25% with evident clinical signs. It is estimated that over 300 million cattle and 250 million sheep in the world that are grazing in areas where infective forms of *F. hepatica* are present, represent annual losses of more than US$ 3 billion (OLAECHEA, 2004; MAS-COMA, 2005). It was also determined that animals can be reduced between 8 and 28% of its body weight when experimentally infected with 40-140 fasciolas, compared with the control group (MALONE; CRAIG, 1990).

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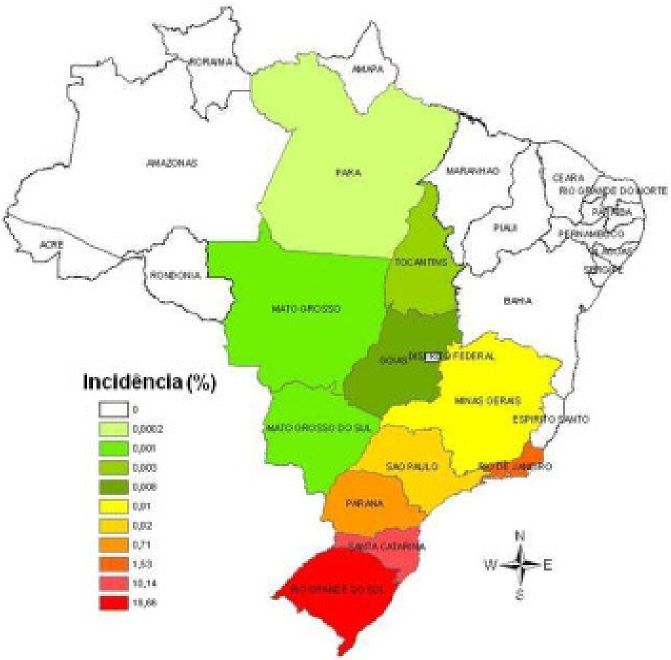
Although there is no assessment of the real economical impact of fascioliasis in Brazil, Lima et al. (2009) determined that 70% of the animals (n=1.251) were positive for *F. hepatica* in stool tests from 16 cities (16/20) of the state of Minas Gerais. Gavinho, Kulek and Molento (2008) determined the prevalence of *F. hepatica* in slaughtered cattle livers between August 2007 and March 2008 when

281.366 animals were slaughtered in Paraná. The authors showed that the city of Castro had the highest number of positive animals, representing 61.6%. It was also shown that 6 beef cattle moderately infected with an average of 35 adult worms, compared to other 6 healthy beef cattle from the same property had an average of 200kg (+/- 5.25) and 212.3Kg (+/- 12.4) of carcass respectively, representing a significant loss of 5.8% (P = 0.004) of the animals' meat or R$ 74.00 (US$ 32.00) per animal.

Figure 1. Map of Brazil and the percentual (%) incidence of *Fasciola hepatica* found in the liver of slaughther cattle inspected by the Federal Inspection Service, MAPA between the years 2003 to 2008 for the municipalities of the South of Brazil.



Source: Elaboration of the authors.

Pathogenesis and Control

Fasciolosis is considered the main cause of liver cirrhosis in ruminants (SERRA-FREIRE et al., 1995). Severe clinical syndromes may be associated with the number of parasites in the liver, its developmental stage, and the presence or absence of *Clostridium novyi* infection. The disease is characterized by ubiquitous clinical signs of liver disease and is more severe in sheep (due to the size of the liver) and the incapacity to acquire natural immune response against the parasite (FORTES, 2004). The main clinical signs of the disease are the gradual reduction of weight, weakness, anemia, hypoproteinemia and subcutaneous edema, particularly in submandibular region and abdomen (BOWMAN, 1995). The abrasion caused by pimples and the action of the pre-setting of *F. hepatica* seems to represent the most damage caused in the liver. The death of the host occurs as a result of bleeding induced by such injuries. The trematode is usually found in histopathology exams *in situ* and in fecal contents when searching for eggs (RIET-CORREA et al., 2001).

Although *F. hepatica* control in ruminants must be perform with preventive treatments under a wide strategic program based on the intermediate host life cycle (ROBERTS; SUHARDONO, 1996). This is certainly not the case in cattle farms in Brazil, where we largely see salvage treatments being used to avoid clinical cases (M. Molento, personal communications). Control measures must be taken to reduce the prevalence of the metacercariae (DALTON, 1999) but the indication to drain (artificially creating channel) areas in endemic areas can also be difficult when these consists of vast irrigation plains for agricultural use (rice, vegetables) (TORGERSON; CLAXTON, 1999). In wetland and marshes, the control of the snail becomes difficult and there is the dependency of effective chemicals, which in turn may cause the selection of a resistant population and impose a major risk for an environmental disaster.

The increase development of techniques for the study of fascioliasis should help to achieve greater efficiency and speed in epidemiology, diagnostic and the prevention of the disease. In this context, the use of PCR (polymerase chain reaction) and ELISA has been validated for their routine use in Brazil. Such techniques may improve the control and treatment indications, as well as assist to monitor the development of resistant parasites.

Zoonotic Disease

Although fasciolosis is considered the main cause of liver cirrhosis in ruminants (SERRA-FREIRE et al., 1995), *F. hepatica* young stages are also harmful to the health of the animals. Severe clinical syndromes may be associated with the number of parasites and its evolution stage, and the presence or absence of *Clostridium novyi* secondary infection. The disease is characterized by classic clinical signs of liver damage (anaemia, prostration) and is more severe in sheep (due to the smaller size of the liver) and their absence of acquired immune response against the parasite (FORTES, 2004). The general clinical signs of the disease are the gradual reduction of weight, weakness, anemia, hypoproteinemia and subcutaneous edema, particularly in the submandibular region and abdomen (BOWMAN, 1995).

Historically, the consumption of raw liver caused infection in humans, especially in Asian countries (SCHACHER; KHALIL; SALMAN, 1965). Boray, Taira and Yoshifuji (1997) stated that human fascioliasis were associated with the ingestion of infected aquatic plants. Busetti (1985) characterized fasciolosis as a family-disease, after describing 30 human cases, where 9 were from the same family and their close neighbors in Paraná. In this study the infection was attributed to raw vegetables intake along with the presence of *L. columella* or *L. viatrix* mollusks. Gabrielli et al. (2014) described a *F. hepatica* outbreak in a Romanian family where 3 people have developed clinical fasciolosis and were diagnosed by cholangiopancreatography and coproparasitological analyses when travelling into Italy.

It is estimated that 17 million people are infected with *Fasciola* sp. in the world, and in countries such as Bolivia, Peru and Egypt, the disease is considered hyper-endemic (ROKNI et al., 2002; MAS-COMA; VALERO; BARGUES, 2009a). In these areas, the high prevalence in humans, over 70% in stool samples and 100% in serology, does not necessarily seem to be related to the high prevalence of fascioliasis in domestic animals (MAS-COMA; VALERO; BARGUES, 2009b). Thus, the parasite seems to be present in the environment and humans are the source of infection to other humans mainly by the complex drinking water/sewage contamination. In Bolivia, young-age kids get contaminated by eating edible plants while taking care of the family herd. So, there is a major World Heath Organization, WHO effort for designing control strategies in high-risk countries where a WHO working group face a massive problem due to the large area, approximately 100 km^2 in Bolivia, of the disease prevalence.

The wide distribution of *Fasciola* sp., which runs from below sea level, as in the Caspian Sea area to up to 4.200m of altitude in the Paso del Condor, Venezuela, has to be with the large capacity of the parasite and its intermediate host in colonizing new areas (GASNIER et al., 2000). And as a typical anthropozoonose, domestic animals species, besides sheep and cattle, can also play an important role as reservoirs for human beings, especially pigs, horses and buffaloes, according to the place and the sanitary system (MAS-COMA; BARGUES, 1997).

The pathogenesis in humans begins with a mild abdominal pain, which may develop to a chronic liver infection. Ultrasound exam or CT scan, especially with heterogeneous hepatomegaly, nodular focal lesions and peripheral branched aspect, predominantly in the right lobe, ascitis and pleural effusion can be used to visualize focal grey lesions. Therapy with triclabendazole (TBZ) a drug that is also approved for veterinary use, is successfully being used in humans in high-endemic areas, once a year in the Altiplano region, Bolivia since 2007, without significant side effects (OLIVEIRA et al., 2002). In this case, more and more Public Health agents are concerned that TBZ-resistance will spread over in humans, by the animal- or by the human way. Several aspects of human fasciolosis were only recently elucidated and the literature on human fascioliasis is scarce compared to the vast list of publications about the animal disease, reinforcing the anthropozoonotic feature of the disease.

Parasite Resistance

The use of anthelmintics in a preventive way, more than 3 times a year, has its effectiveness discussed, since there have been reports of TBZ resistance (TBZ-r) in Australia (BOWMAN, 1995), Ireland, United Kingdom, Netherlands and Spain (FAIRWEATHER, 2005) and more recently in Brazil (OLIVEIRA et al., 2008). Even though, Boray and Fairweather (1999) tested the efficacy of several anthelmintic compounds against *F. hepatica*, and TBZ presented to be the best drug, Oliveira et al. (2008) determined a reduction efficacy of TBZ after an outbreak of *F. hepatica* in sheep and goats in Almirante Tamandare, PR, Brazil. Stool analysis revealed that curative treatment with this drug had an efficacy of 66.3 and 57.3% in sheep and goats, respectively. TBZ is the drug of choice for infected animals killing young and adults forms of the parasite. The drug belongs to the benzimidazole family and acts selectively at the cells' β-tubulin, depolarizing microtubules, causing a loss of its function in helminths (ROBINSON et al., 2001).

The molecular benzimidazole mechanism of resistance has been demonstrated to be the replacement of the amino acid phenylalanine to tyrosine, in the position 200 of the β-tubulin isotype 1 molecule (ROBINSON et al., 2004) but that is not fully accepted because sequences of β-tubulin cDNA from TBZ-susceptible and –resistant flukes may not have differences between their respective primary amino acid sequences (FAIRWEATHER, 2005). The selection of genes that are involved in drug resistance is a concern where sheep is regularly treated with TBZ, especially in farms where cattle share the same pastures. Therefore, drug selection might migrate to cattle imposing a different health risk (MOLL et al., 2000).

TBZ is also the treatment option for humans but so far no resistance to this drug has been documented in human cases, although it is possible that animals serves the reservoir and source of TBZ-r infection (BRENNAN et al., 2007).

Molecular Diagnostics

Several applications for using molecular biology techniques have been developed for the study of the genetics, diagnostics and drug resistance in veterinary parasitology (PRICHARD, 2001; VON SAMSON-HIMMELSTJERNA; BLACKHALL, 2005; GILLEARD; BEECH, 2007). The polymerase chain reaction (PCR) is a tool that has been used in the differentiation of the two species of flukes in Egypt (EL-GOZAMY; SHOUKRY, 2009) tracking the possible nucleotide polymorphisms of the parasites. PCR is also used in the identification of intermediate/hybrids between *F. hepatica* and *F. gigantica* (LI et al., 2009).

PCR has been used for the identification of *F. hepatica* making it possible to determine resistance markers for diagnosis (FAIRWEATHER, 2005). Robinson et al. (2001) determined that *F. hepatica* has only one β-tubulin gene, however, is necessary to determine the possible variability of the cDNA of β-tubulin between various isolates. In relation to drug resistance, many isotypes of α and β-tubulin were identified and their coding regions sequenced. After comparison, β-tubulin sequences of susceptible and resistant parasites, revealed that the resistant isolate contained all three mutations of the nucleic acids involved in resistance to benzimidazole resistance (200, 196 and 198) (BRENNAN et al., 2007).

The development of molecular protocols with multiple functions are helping to identify new species of *Lymnaea* sp. that are essential for epidemiological studies. Carvalho et al. (2004) used PCR-RFLP directed to the first and second internal transcribed spacer (ITS1 and ITS2) of rDNA and to 16S mitochondrial ribosomal gen (16S rDNAmt) using 12 restriction enzymes to identify *L. columella*, and *L. viatrix*, *L. diaphana* in different locations in Brazil, Argentina and Uruguay. This analysis showed typical patterns of *L. columella* and *L. diaphana*, which were consistent with classic morphological characteristics, but *L. viatrix* demonstrated six different profiles, complicating the identification of the species. The Real-time PCR has proven to be faster, more reliable, and more specific than conventional methods to distinguish morphologically similar variants of a broad spectrum of taxa (WATANABE et al., 2004, ITOI et al., 2005).

Serological Diagnosis

The efficacy of drugs may be assessed by post-mortem examination of the liver and by counting *F. hepatica* eggs in feces (WOOD et al., 1995), but these methods are expensive and laborious (MOLLOY et al., 2005). Serological tests for the diagnosis of infection by *F. hepatica* were developed (SANCHEZ-ANDRADE et al., 2000) and are an alternative diagnostic to indirect methods of assessing the effectiveness of control methods. The advantages of the serological analysis are outstanding, since early chemical intervention reduces tissue damage caused by the migration of immature stages of the parasite and the fecal excretion of eggs by the hosts (MOLLOY et al., 2005). However, the use of serological tests for evaluating the effectiveness of chemotherapy may be problematic because such assessments are usually based on the degree to which faecal egg counts were reduced. Beside this, the recognition of serum IgG specific to *Fasciola* sp. might persist for long periods, even after the removal of the parasites of the liver (SANCHEZ-ANDRADE et al., 2002).

Early diagnosis of fascioliasis (during the prepatent period) using tests for the detection of antibodies may be essential to prevent the negative impact of the disease on productivity (SANCHEZ-ANDRADE et al., 2000; DIXIT; YADAV; SHARMA, 2004). Among the immunodiagnostic tests available, the enzyme linked immunosorbent assay ELISA is widely recommended for epidemiological studies (BOSSAERT et al., 2000).

More recently, the use of raw milk for the diagnosis and monitoring of diseases in cattle became routine with tests for *Ostertagia* spp., *Dictyocaulus* spp., and *Cooperia* sp.. The evaluation of antibodies in milk accomplishes an important role for the implementation of control and treatment strategies, including in eradication programs of fasciolosis in many countries (PRITCHARD 2001; PRITCHARD; KIRKWOOD; SAYERS, 2002). It has been demonstrated a good correlation between the diagnosis in milk and titles of serum antibodies in animals (MOLLOY et al., 2005; PRITCHARD 2001; PRITCHARD; KIRKWOOD; SAYERS, 2002) even during different seasons. Charlier et al. (2009) found seasonal differences in the levels of specific antibodies to *F. hepatica*, but not to *Ostertagia ostertagi*. Specific antibody levels for *F. hepatica* were higher in spring and fall, as this pattern was expected because the epidemiology of the trematode, since adult parasites are more prevalent in the winter months.

Bernardo et al. (2013) reported in a comparative study of the commercial ELISA kit with stool examinations that in endemic areas, despite the increased detection of animals positive for *F. hepatica*, the stool examinations was still recommended due its high practicality, lower cost and easiness of execution. The great advantage of sampling milk is the ease of obtaining the sample compared to the invasive form (the collection of blood and/or faeces). In England and in Wales the number of diagnosed cases of fasciolosis in cattle increased significantly, especially in dairy cattle, although most chronic infections were diagnosed by the egg count method (SALIMI-BEJESTANI et al., 2005).

Geographic Information System (GIS)

The Geographic Information System (GIS) allows the analysis of complex information by integrating data from multiple sources, creating a georeferenced database. In a country of continental dimensions such as Brazil with considerable information deficiencies to assist in decision-making towards the control of diseases (leishmaniasis, schistosomiasis, fascioliasis) GIS may represent an essential support tool (CARNEIRO et al., 2007).

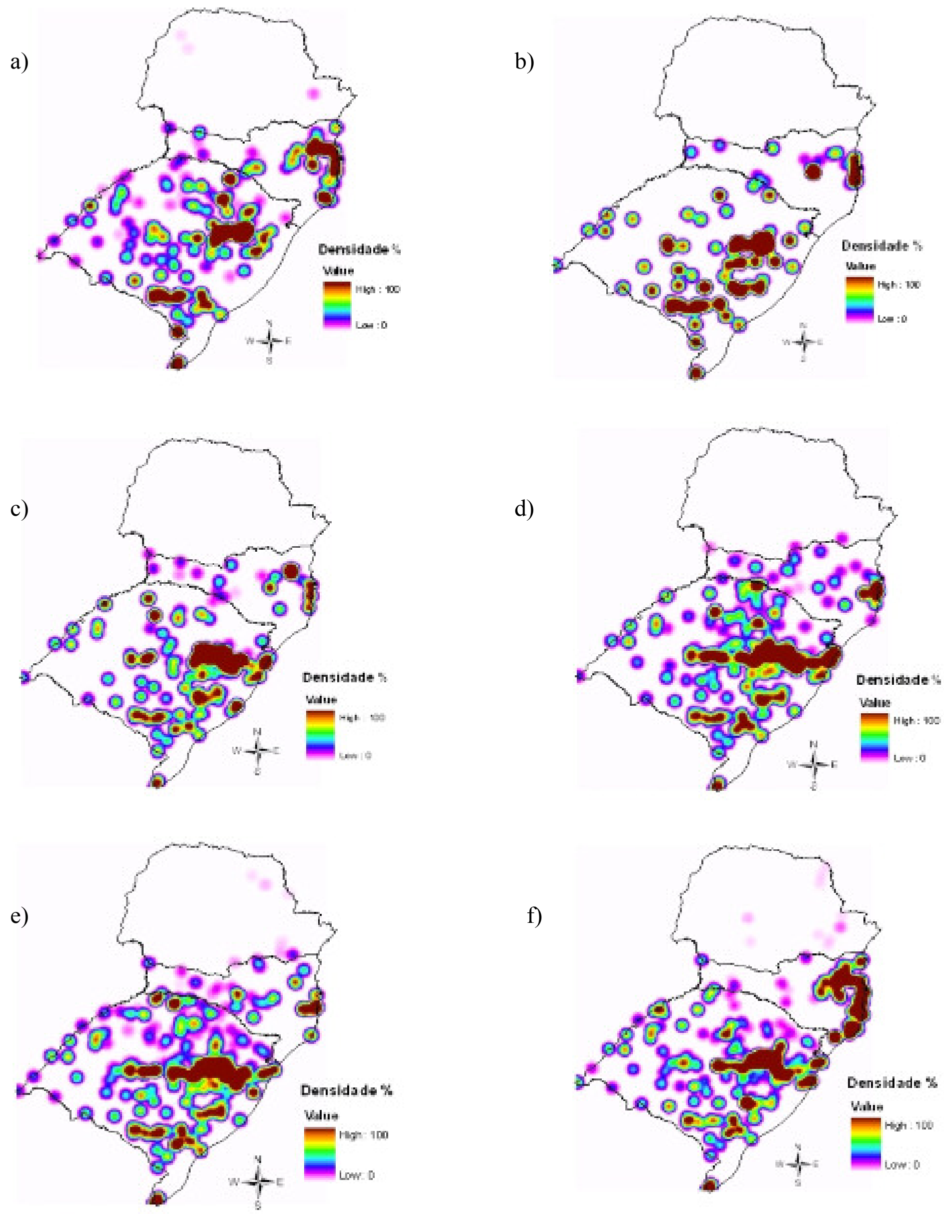
The software that performs geoprocessing tasks are designed to correlate information of a particular event, a disease, to a geographic location of its occurrence, creating epidemiological maps for viewing and evidencing risk factors. The Software technology itself may have a relatively low cost, but the major problem is the access to reliable databases. In Brazil, the best databank are provided by the Brazilian Institute of Geography and Statistics, IBGE; the Ministry of Science and Technology, MCT; the Ministry of Agriculture, MAPA; the Ministry of Health, MS; and the Brazilian Company of Agricultural Research, EMBRAPA. The images may have different definition quality, approximation and other details, such as temperature, humidity, topography, hydrology and forms of occupation; agricultural or human (IBGE, 2006). Currently, data about climate and the environment have been widely used in studies of distribution and frequency of certain diseases in Tropical areas using GIS. An important issue about the use of these analyzes is the comprehension about the population behavior with respect of possible changes in the environment (CROMLEY, 2003).

In the last decade, a series of studies using GIS have demonstrated the real importance of this resource in the generation of knowledge about the epidemiology of several diseases (FUENTES, 2004). The epidemiological reason to use GIS is to allow the development of spatial and temporal models to map fascioliasis permitting the classification of the transmission into low, moderate or high-risk areas to coordinate the implementation of control activities (FUENTES; SAINZ-ELIPE; NIETO, 2005). GIS has been used to produce models to predict the risk and to evaluate fasciolosis in East Africa (MALONE et al., 1998), Ethiopia (YILMA; MALONE, 1998), The United States (ZUKOWSKI; WILKERSON; MALONE, 1993) and more recently in Brazil (DUTRA et al., 2010; SILVA, 2012). Cringoli et al. (1996, 2000 and 2001) used GIS in a territory parasitological analysis to plan sampling procedures in a limited geographical area and to quickly create maps of parasite distribution. Cringoli et al. (2002) using GIS showed a spatial distribution of *F. hepatica* infection in Campania, Puglia and Basilicata, region located in southern Italy, characterized as a mountainous area with altitudes levels of 100 to 1000m above sea level. The region had few rivers or streams and no swamps or lakes. However, there were in the region positive cases with low concentration of snails and presence of cattle and sheep infected on the farms. As the water supplies in the study area were generally ephemeral, positivity for fascioliasis was attributed to the surrounding vegetation, which provided a constantly humid environment favoring the risk.

Malone et al. (1998) and Tum et al. (2007) validated risk maps for *F. hepatica* in Cambodia considering environmental factors favorable to the life cycle of the intermediate host, determining the risk of the disease. Sometimes, the boundaries of the environmental areas are not strictly fixed and may vary considerably due the weather and other environmental components. This is expected where small environment changes occur such as the annual weather variations (MALONE et al., 1998). Silva et al. (2011) analyzed the spatial distribution of bovine fasciolosis in the State of Santa Catarina, Brazil for 2006 and assessed the correlation between high rates of fasciolosis with precipitation and altitude. Firstly, the Positivity Index (Pi) of slaughtered animals and spatially distributed throughout the state. Next, the authors selected only cases with Pi > 50% and analyzed its relationship with the precipitation variables from the Integrated Environmental Information System for Environmental Health, and altitude, generated from the Shuttle Radar Topographic Mission, SRTM. Although the results between fasciolosis and altitude did not show a high correlation, it was observed that the percentage of disease was higher in cities where the altitudes were lower. And more, the correlation between fasciolosis and precipitation suggested that there is a tendency of fasciolosis to increase, as the volume of precipitation is high.

The Kernel analysis or Kernel intensity estimator is a tool built in some geoprocessing softwares that estimate the number of events per unit area in each cell of a regular grid of the study area (BAILEY; GATRELL, 1995). The technique reduces the variability of the data and also retains the essential site characteristics (ARAÚJO et al., 2007). The degree of variability is controlled by choosing a parameter known as the 'bandwidth', which indicates the area to be considered in the calculation and the geographic range of the event of interest (SOUZA; CARVALHO, 2000). Figure 2 shows the use of Kernel intensity estimator to study the epidemiology of *F. hepatica* based on its focal occurrence during 2003 to 2008 in the Southern states of Brazil. It is notable that some regions on the coast of Santa Catarina and the Center and the South of Rio Grande do Sul had a considerable high prevalence of the infection. It is also possible to note that even looking into a six-year period, there were no significant changes in the infection rate in cattle in all 3 states, suggesting a strong and fixed habitat for *F. hepatica* occurrence.

Figure 2. Density of infected livers with *Fasciola hepatica* using the Kernel analysis. Data provided by the Federal Inspection Service, MAPA between the years a) 2003; b) 2004; c) 2005; d) 2006; e) 2007; and f) 2008 for the municipalities of the South of Brazil.



Source: Elaboration of the authors.

Although the epidemiological maps reported in this review article have been created with cattle data, the risk of human infection may also be taken from them. Thus, an endemic area for fasciolosis in animals can represent favorable conditions for the occurrence of the disease in humans. To better illustrate this information, all major cities of Santa Catarina (Joinvile, Blumenau, Florianópolis, Itajaí) and Rio Grande do Sul (Porto Alegre, Canoas, Santa Maria, Pelotas) falls within the incidence area of fasciolosis in cattle, exhibiting an overlap potential risk area for humans.

Climate Changes

Climate changes can be understood as any change in the weather (temperature) or precipitation (rain) throughout the years, due to natural variability or as result of a large pressure of human activity. Published scenarios to describe possible effects that climate change will have over the earth have been created to elucidate a variety of situations, including interactions between vectors and pathogens (BARRET et al., 1998). Mas-Coma, Valero and Bargues (2009a) studied the impacts that climate change could cause on the larval forms of trematodes and their intermediate hosts, concluding that flukes are affected by climate change, mainly due to their peculiar evolutionary characteristics and strong interdependency.

The seasonality of fascioliasis is closely linked to the effects of rainfall and temperature, where even few changes on these factors may directly affect the life cycle of both intermediate hosts and the parasite (ROJO-VAZQUEZ et al., 2012). Ollerenshaw and Rowlands developed in 1959, for the first time, a model for predicting the risk of bovine fascioliasis based on climatological data (HOPE-CAWDERY; TALUNTAIS; LEITRIM, 1981). Kenyon et al. (2009) in a review about how climate change would affect the epidemiology of *Haemonchus contortus, Nematodirus battus, Teladorsagia circumcincta* and *F. hepatica* observed that increases in the temperature might negatively influence the regional production of sheep in Scotland. Fox et al. (2011) validated a predictive model for the risk of *F. hepatica* in the United Kingdom and observed high levels of risk for the disease with serious epidemics in the country until the year 2050.

Final considerations

Although fasciolosis is still considered a neglected disease by WHO in humans, there is extensive literature about the diagnosis and control of animal fasciolosis and its relation to the intermediate host. Recent reports regarding the importance of this disease as anthropozoonosis has attracted great attention worldwide. However, the major concern is the wide margin of human and animal unreported cases, which indicates the need of more large-scale accurate diagnoses.

The molecular biology techniques with the next generation sequence and genotyping equipment and the use of satellite images together with information about the weather, will allow a much better understanding of the spatial and temporal distribution associated with *F. hepatica*. The combination of these methods shall facilitate the planning for prevention and control strategies at city and farm level, ensuring improved risk assessment, enabling efficacious decision-making programs using a modern systematic approach.

In Brazil and other countries, the better knowledge of the occurrence of fasciolosis in animals will permit to embrace the concept of One World – One Health, encompassing human and animal health and environment conditions to monitor the dispersion of fasciolosis.

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