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The parasitic phase of *Ostertagia ostertagi*: quantification of the main life history traits through systematic review and meta-analysis

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ABSTRACT

Predictive models of parasite life cycles increase our understanding of how parasite epidemiology is influenced by global changes and can be used to support decisions for more targeted worm control. Estimates of parasite population dynamics are needed to parameterize such models. The aim of this study was to quantify the main life history traits of *Ostertagia ostertagi*, economically the most important nematode of cattle in temperate regions. The main parameters determining parasite density during the parasitic phase of *O. ostertagi* are (i) the larval establishment rate, (ii) hypobiosis rate, (iii) adult mortality and (iv) female fecundity (number of eggs laid per day per female). A systematic review was performed covering studies from 1962 to 2007, in which helminth-naïve calves were artificially infected with *O. ostertagi*. The database was further extended with results of unpublished trials conducted at the Laboratory for Parasitology of Ghent University, Belgium. Overall inverse variance weighted estimates were computed for each of the traits through random effects models. An average establishment rate (±S.E.) of 0.269 ± 0.022 was calculated based on data of 27 studies (46 experiments). The establishment rate declined when infection dose increased and was lower in younger animals. An average proportion of larvae entering hypobiosis (±S.E.) of 0.041 (±0.009) was calculated based on 27 studies (54 experiments). The proportion of ingested larvae that went into hypobiosis was higher in animals that received concomitant infections with nematode species other than *O. ostertagi* (mixed infections). An average daily adult mortality (±S.E.) of 0.028 (±0.002) was computed based on data from 28 studies (70 experiments). Adult mortality was positively correlated with infection dose. A daily fecundity (±S.E.) of 284 (±45) eggs per female was found based on nine studies (10 experiments). The average female sex ratio of *O. ostertagi* based on individual animal data ($n = 75$) from six different studies was estimated to be 0.55. We believe that this systematic review is the first to summarise the available data on the main life history traits of the parasitic phase of *O. ostertagi*. In conclusion, this meta-analysis provides novel estimates for the parameterization of life cycle-based transmission models, explicitly reports measures of variance around these estimates, gives evidence for density dependence of larval establishment and adult mortality, shows that host age affects larval establishment and, to our knowledge, provides the first evidence for *O. ostertagi* of a female-biased sex ratio.

1. Introduction

Ostertagia ostertagi is one of the most prevalent gastro-intestinal roundworms of cattle in temperate regions and places major constraints on productivity (Charlier et al., 2009). Because climate and farm management drive this parasite's epidemiology, global change affecting both factors could increase challenges to the future control of *O. ostertagi* (Morgan et al., 2013). Predictions of climate change, including increasing ambient temperature in temperate regions, are expected to affect parasite development and survival, resulting in altered infection levels (Semenza and Menne, 2009; van Dijk et al., 2010; Molnár et al., 2013). In addition, intensification of modern dairy farming leads to a wide range of alterations relating to management of nutrition, housing and grazing patterns (Herrero and Thornton, 2013) that may result in

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changes to infection pressure and seasonal patterns of exposure of livestock to infective stages. Besides these changes that affect parasite transmission and epidemiology, increasing reports of anthelmintic resistance strengthen the need for alternative and innovative approaches to parasite control (Kenyon and Jackson, 2012; Höglund et al., 2013).

Mathematical models of infectious diseases have great potential to provide improved understanding of disease epidemiology and factors affecting it (Altizer et al., 2006; Woolhouse, 2011). Also, such models are increasingly applied to nematode control in ruminants with the ultimate goal to support the development of practical parasite control strategies (Smith et al., 1987a; Learmount et al., 2006; Ward, 2006a, 2006b; Grassly and Fraser, 2008; Chaparro and Canziani, 2010). In the past, several mechanistic models based on the life cycle of *O. ostertagi* were developed (Gettinby et al., 1979; Gettinby and Paton, 1981; Smith and Grenfell, 1985; Grenfell et al., 1987a,b; Smith et al., 1987a).

A major limitation of mechanistic models of parasite life cycles is parameter estimation. Where there is significant parameter uncertainty, models frequently make use of expert knowledge, or scale parameters derived from fits of predicted outputs with observed data (e.g. Dobson et al., 2011; Chaparro et al., 2013). While expedient, these approaches are vulnerable to changing conditions, such that the relationships that underpinned inference under specific conditions no longer hold in different places or times, including under future global change scenarios. There is therefore a strong and ongoing need for thorough, transparent and unbiased estimation of key life history parameters, in order to properly inform models of parasite dynamics. Explicit reporting of uncertainty around such estimates is also valuable in guiding and prioritising future experiments. While systematic review and meta-analysis are core methods in biological, medical and veterinary sciences, and are gaining increasing traction in a wide range of subjects (Lean et al., 2009), their use in estimating parameters for parasite transmission models has, to date, been limited.

Parasite density during the parasitic phase of *O. ostertagi* and egg output are functions of four main life history traits: (i) larval establishment, (ii) hypobiosis, (iii) adult mortality and (iv) female fecundity (Fig. 1). Because acquired immunity is known to modulate these traits (Claerebout and Vercruysse, 2000), factors related to development of immunity, such as duration of exposure, intensity of infection and host age, need to be taken into account when quantifying life history traits of the parasitic phase. Former transmission models of *O. ostertagi* used trait estimates that were based on a limited number of experiments to parameterize the parasitic phase (e.g. Anderson and Michel, 1977; Gettinby et al., 1979; Smith and Grenfell, 1985). During recent decades many infection trials with *O. ostertagi* were performed for various purposes (e.g. drug efficacy trials, host-parasite interaction studies). These studies enable us to make new estimates based on a larger number of experiments. Future transmission models will benefit from more accurate estimates of these parameters and their variation, but to date no attempt has been made to collect and summarise the available literature.

The aim of this study was to (i) quantify the main life history traits of the parasitic phase of *O. ostertagi* and (ii) assess potential influences associated with the effect of immunity on these traits. A systematic review and a meta-analysis were performed covering studies from 1962 to 2007 in which helminth-naïve cattle were artificially infected with *O. ostertagi*.

2. Materials and methods

2.1. Parameter definition

The four main life history traits of the parasitic phase of *O. ostertagi* addressed in this study are (i) the larval establishment rate, (ii) the hypobiosis rate, (iii) adult mortality and (iv) female fecundity (Fig. 1). Table 1 provides the definitions for these traits as used in this study.

2.2. Search strategy and eligibility criteria

Peer-reviewed publications were the major sources for data collection. In addition, data from former unpublished studies carried out at the Laboratory of Parasitology (Ghent University, Belgium (UGent)) were collected and added to the database. These latter data were generated in the context of *O. ostertagi* vaccination or anthelmintic efficacy research. They are further referred to as 'UGent trial (1–7)'.

For the systematic review, the electronic database ISI Web of Science was explored using the following general keywords: (cattle OR bovine OR cow OR heifer OR bull OR steer OR calf OR calves) AND (nematode OR helminth OR parasit* OR trichostrongyl* OR ostertag* OR Cooperia OR oncophora) AND (infect* OR transm*). No restrictions were placed on publication year or language. The search was performed for items published on or before February 6, 2012. The obtained literature was first subjected to a title-based selection, followed by a second selection based on reading of the full text. All studies in which naïve bovines were artificially infected with *O. ostertagi* using single or trickle infection protocol, were considered eligible on the conditions that (i) no anthelmintic treatment was applied during the infection and (ii) they reported abomasal worm counts (individual or aggregated) after necropsy with an associated measure of variance (i.e. S.D., S.E.M.).

To extract data for the quantitative analysis, specific eligibility criteria were used for each life history trait. For the calculation of larval establishment and hypobiosis, only studies in which the duration of infection (i.e. time period between first infection and

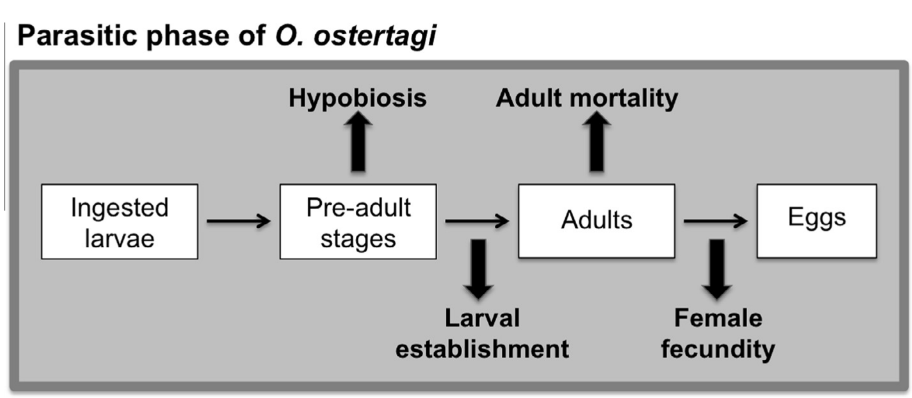

Fig. 1. Schematic overview of the parasitic phase of *Ostertagia ostertagi* and its main life history traits.