BIODIVERSITY AND EXTINCTION *VERSUS* CONTROL OF OESTRID CAUSING MYIASIS IN MEDITERRANEAN AREA

OTRANTO D.* & COLWELL D.D.**

Summary:

Oestrid larvae causing myiasis display a wide degree of biodiversity, in terms of species of domestic and wild mammals infected and anatomical sites. The presence in some regions of southern Europe of a high number of different species of oestrids in domestic animals stimulated interest in exploring the basis of such degree of parasitic biodiversity in the Mediterranean region. However, broad spectrum anti-parasitic treatments (e.g. macrocyclic lactones) constitute a critical factor for the selection of species of Oestrids and for the maintenance of their biodiversity in a given area. The dynamic equilibrium that oestrid larvae have established with the host and the environment as well as the span of biodiversity they represent may be considered to be at odds with maintaining animal welfare and reducing animal production losses.

KEY WORDS : Oestridae, myiasis, biodiversity, extinction.

The dipteran Family Oestridae includes about 150 species of flies (botflies) (Zumpt, 1965) whose larval stages are obligate parasites living in the hosts' tissues or organs, causing what is commonly known as myiases. While larvae belonging to the sister groups Calliphoridae and Sarcophagidae (blowflies and fleshflies) cause myiases of short duration (larval development is usually completed within 4-7 days), which are generally localized at the host's body orifices or in wounds, larval oestrids live for weeks to months in their associated hosts (reviewed in Hall & Wall, 1995). Indeed, oestrid larvae are intimately associated with their hosts, living and feeding in the host's nasopharyngeal tract (subfamily Oestrinae eg. *Oestrus ovis*, *Rhinoestrus purpureus*, *Cephalopina titillator*), gut system (subfamily Gasterophilinae eg. *Gasterophilus* spp. in horses) and internal organs as well as in subcutaneous tissues (subfamily Hypodermatinae eg. *Hypoderma bovis* and *Hypoderma lineatum* in cattle and *Przhevalskiana silenus* in goat).

While the most well known species are those affecting animals important to human endeavours, the majority of oestrid species parasitizes wildlife hosts. These include well known and showy species such as elephants, giraffes and rhinoceros as well as many less prominent hosts such as mice (reviewed in Colwell *et al.*, 2006). Oestrid myiases are characterised by low level of pathogenicity, a high degree of host specificity and the larvae exhibit a variety of morphological and biological adaptations which together indicate a long period of time since their divergence from a common ancestor (Papavero, 1977; Pape, 2001). This evolution occurred in different environments under specific circumstances and, consequently, oestrid distribution in a geographical area is affected by a wide variety of factors linked to their biology and relationship they have established with their host/s and environment.

Despite having a minor pathogenic effect and thus not inducing significant mortality and loss of morbidity, oestrid myiases may have severe economic impact on the livestock industry in developing and developed countries through abortion, infertility, reduction of milk production, and weight gain as well as reducing the value of hides (reviewed in Hall & Wall, 1995). Although the impact of myiases on livestock production is difficult to quantify, these parasitic infections have long been considered a major veterinary concern. Thus over the past 30' years research on myiases has mainly focused on development of synthetic chemical control products. Recent reports of the presence of an unusually high number of different species of oestrid larvae causing myiasis (Table I) in domestic animals in some regions

Genera	Site of parasitism	Disease	Parasitized animals
Oestrus ovis	Nasopharynx	Nasal botfly or Oestrosis	Sheep, goat, humans
Gasterophilus spp.	Digestive tract	Gasterophilosis	Horse, donkey
Hypoderma bovis, *H. lineatum*	Dermis and internal organs	Bovine hypodermis	Cattle, horse, humans
Przhevalskiana silenus	Subcutaneous tissue	Coat warble fly infestation	Goat

Table I. – Oestrid myiasis-causing larvae whose presence was recorded in the Mediterranean region: species, name of caused disease and animal host species affected.

* Department of Veterinary Public Health, University of Bari, 70010, Valenzano (Bari), Italy.
** Agriculture & Agri-Food Canada, Lethbridge Research Centre, Canada.
Correspondence : D. Otranto.
Tel./Fax: +39 080 5443839 – E-mail: d.otranto@veterinaria.uniba.it

of southern Europe (Principato, 1984; Otranto *et al.*, 2004; Otranto *et al.*, 2005a), stimulated interest in exploring the basis of such a high degree of biodiversity in this area and in discussing the reasons for the reduction of these parasitic infections in animals. While preservation of biodiversity is considered an important goal and parasite reduction to levels of economic insignificance is preferable to eradication, it appears to be at odds with concept of maintaining animal welfare and reducing animal production losses.

OESTRID BIODIVERSITY IN THE MEDITERRANEAN BASIN

The most common myiases spread throughout the Mediterranean basin were cattle and goat hypodermoses, sheep nasal oestrosis and equine gasterphilosis (Table I). Some of the most relevant factors that may have contributed to the presence of such an unusual high number of different species of oestrid in domestic animals include animal management (e.g. free grazing animals that remain untreated thus harbouring a number of endo- and ecto- parasites), the Mediterranean climate that is favourable to the development of the biological cycle of several oestrids and ecological factors (extensive pastures are shared by animals of different farms). For example, in Mediterranean Countries goat breeding is a very important activity not only for meat, milk and cheese production but also because this species can utilise vast areas of marginal land not suitable for other ruminants. In addition to this there are also historical aspects that may have contributed to the number of oestrid species. A hypothesis presented by Otranto *et al.* (2006) suggests that as a major migratory crossroad for numerous human movements throughout history this region became a repository of not only their domestic animals, but their accompanying parasites.

Reports from central (Principato *et al.*, 1984) and southern (Otranto *et al.*, 2005a) Italy indicated that horses and other domestic animals (e.g. cattle and small ruminants) are affected by different species of oestrids. Specifically, horse gastrointestinal myiasis (by larvae of *Gasterophilus* spp. flies) which has a worldwide distribution is primarily caused by larvae of *Gasterophilus intestinalis* and *Gasterophilus nasalis* (Zumpt, 1965; Drudge *et al.*, 1975; Lyons *et al.*, 1994). Other species *i.e. Gasterophilus inermis*, *Gasterophilus pecorum* and *Gasterophilus haemorrhoidalis*, were reported only occasionally in very limited areas of Eastern European countries (Zumpt, 1965). All the five species have been reported both in central (Principato *et al.*, 1984) and, more recently, in southern Italy (Otranto *et al.*, 2005a). Co-occurrence of five different species of *Gasterophilus* affecting horses in these areas is of ecological interest as it represents the highest biodiversity of this genus at any locality. Retrospective comparison of the prevalence of five species of *Gasterophilus* recently recorded in Italy (Otranto *et al.*, 2005a) with data available from four seasons of observation (1983 -1986) in central Italy (Principato, 1989), shows that the number of *G. inermis*, *G. pecorum* and *G. haemorrhoidalis* has been decreasing relative to *G. intestinalis* and *G. nasalis*. Whether this trend is likely to continue, leading ultimately to the extinction of the three former species of *Gasterophilus*, or whether a new equilibrium of species composition and abundance will be reached, is for the moment unclear. Another myiasis of horses that has been firstly reported in Europe, specifically in southern Italy is the nasal myiasis by *Rhinoestrus* spp. (Otranto *et al.*, 2004). The low prevalence of *Rhinoestrus* infections worldwide recorded in the last few years indicates a changing pattern of prevalence of this species of fly. Oestrids that cause myiasis in ruminants are still present in a few countries of the Mediterranean basin despite their disappearance from other core areas of their historical ranges (see above). For example, the presence of *H. lineatum* (cattle grub) has been drastically reduced over the last thirty years as a result of eradication programmes in some countries (see above, reviewed in Boulard, 2002). Finally, a typical example of a myiasis that was previously widespread in southern Italy with infestation rate exceeding, in some areas of Italy, the 70 % of flocks (reviewed in Giangaspero & Lia, 1997) and that has almost disappeared is goat warble fly infestation (caused by larvae of *P. silenus*). Nowadays, *P. silenus* is confined to small areas of southern Italy (Apulia and Calabria regions) (Otranto & Puccini, 2000) and of Greece (Papadopulos *et al.*, 1997).

THE CONTROL OF MYIASIS: THE SUCCESS OF CHEMICALS

From the middle of the last century control of oestrids myiasis in livestock, in particular warble fly infestation, or cattle grub, relied on the use of several drugs in different formulations. The first compounds which gave excellent control were the organophosphate based products (OPs) which, however, have produced some unsatisfactory results in terms of animal and human safety and efficacy (Boulard, 1979; Ziv *et al.*, 1988; Charbon & Pfister, 1993). In the past few years OPs have been superseded by macrocyclic lactones such as ivermectin (Sutherland, 1990), or similar compounds such as moxidectin (Lonneux & Losson, 1994) and eprinomectin (Holste *et al.*, 1998). In particular, ivermectin has proved to be highly effective against *Hypoderma* spp. larvae even at dosages as low as 0.2 µg/kg, which is 1/1000th of the recommended dose (Drummond, 1984). Consequently, injectable or pour-on ivermectin formulations have been used for nationwide control of cattle hypodermosis in several European countries (reviewed in Boulard, 2002) thus reducing the prevalence of the infestation to 0.5 % and in some cases eradicating it altogether, as in the United Kingdom, Ireland and Denmark (Argenté, 1992; O'Brien, 1998). Recently, moxidectin (Cydectin®, Fort Dodge) injectable and *pour-on* formulations showed to be useful in a pilot control program against bovine hypodermosis in Southern Italy and contributed to significantly reducing infestation rates in that area (Otranto *et al.*, 2005b). The exquisite sensitivity of cattle grubs, and other similar species to the macrocyclic lactone products raises the very real possibility of regional extinction. The high host specificity of these species coupled with absence of any non-domestic animals reservoirs in the Mediterranean basin, such as exist for the reindeer warble in northern latitudes, will make this event even more likely.

WHEN THE EVOLUTION OF A PARASITE MAY REPRESENT A FIRST STEP TOWARD ITS EXTINCTION: CO-EXTINCTION

It has been recently discussed that oestrid coevolution with their hosts has played a major role in their speciation (Stevens *et al.,* 2006). Consequently, the various species are highly specialized, having developed a number of ecological strategies (e.g. adult fly lekking behaviour) that ensure efficient breeding and host location. In addition, larvae are specifically adapted to a parasitic existence in "their own host" as indicated by the biological, physiological and biochemical strategies they have evolved to cope with non-specific (NK cells, complement) and/or specific (antibodies and T-lymphocytes) immunological responses of the host (reviewed in Otranto, 2001). The larval biochemical mechanisms above represent "highly evolved systems" for the parasite to spread through a host population. However, the strict host affiliation of oestrids and the absence of other competent hosts may represent a first step toward their extinction associated with definitive host disappearance (e.g. rhinoceros or elephants).

DISCUSSION

Although no specific data are reported on the likely disappearance of oestrid myiases in the Mediterranean area, retrospective examination of the scientific literature indicates that oestrids are approaching a definitive extinction end point. This phenomenon has not only been an effect of broad spectrum anti-parasitic treatments but also of the reduction in the number of animals, managed under free range husbandry schemes, which act as reservoirs for oestrids. The "conflict" between the preservation of the span of oestrid biodiversity and the reasons of maintaining animal welfare may be considered as an example for the conflict between preservation of parasitic biodiversity and increasing animal production thus producer income from livestock. The above conflict, in a broader philosophic way, could involve the struggle of science/knowledge vs. the animal production and economic reasons. This conflict comes into play while planning control strategies for oestrids (e.g. by management or eradication) considering that many aspects of oestrid biology and ecology still remain unknown. As a result many of the poorly known species of oestrids, for which little knowledge of biology and host parasite relationships exists, are only preserved in the collections at the Zoological Institute Museum of the Russian Academy of Sciences in St. Petersburg (Russia) or at the Natural History Museum in London (UK). Even in these collections many oestrid larvae languish while others have not been studied or, in most cases, seen for decades. Have they lost their only opportunity to be known to this world?

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