

DO LAGOMORPHS PLAY A RELAY ROLE IN THE EVOLUTION OF THE TRICHOSTRONGYLINA NEMATODES?

AUDEBERT F.*,** & DURETTE-DESSET M.C.*

Summary:

In order to confirm or refute the relay role of lagomorphs in the evolution of the Trichostrongylina (Nematoda), the following points were studied by summarizing previous works on the subject: the chronology of the life cycles (27 conducted in natural hosts, lagomorphs, ruminants or arvicolin rodents; 14 in experimental hosts); the parasitic phase in the experimental host and the adaptation involved; the migration of the parasites into the tissues of the host; the morphogenesis of larval stages and molecular phylogeny. These data confirm, in their entirety, that lagomorphs may be considered as "relay" hosts in the evolution of the Trichostrongylina.

KEY WORDS : Nematoda, Trichostrongylina, relay role, lagomorphs, ruminants, arvicolin rodents.

Résumé :

LES LAGOMORPHES ONT-ILS JOUÉ UN RÔLE DANS L'ÉVOLUTION DES NÉMATODES TRICHOSTRONGYLINA ?
Pour confirmer ou infirmer le rôle relais des Lagomorphes dans l'évolution des Trichostrongylina (Nematoda), les points suivants ont été étudiés en synthétisant les travaux précédents sur le sujet : la chronologie des cycles biologiques (27 cycles ont été réalisés chez l'hôte naturel, Lagomorphes, Ruminants ou Rongeurs Arvicolinae; 14 chez l'hôte expérimental); la phase parasite chez l'hôte expérimental et l'adaptation qui en découle; la migration des parasites dans les tissus de l'hôte; la morphogenèse et la phylogénie moléculaire. Toutes ces données confirment que les Lagomorphes peuvent être considérés comme des hôtes "relais" dans l'évolution des Trichostrongylina.

MOTS CLÉS : Nematoda, Trichostrongylina, rôle relais, Lagomorphes, Ruminants, Rongeurs Arvicolinae.

INTRODUCTION

Among parasitic nematodes infesting terrestrial vertebrates, the Trichostrongylina are one of the largest groups, widespread throughout the world. The classification of this group, which is mainly based on morphological characters and their evolution, was proposed by Durette-Desset & Chabaud (1977, 1981) and improved by Durette-Desset (1985) with the addition of some biological and ecological data. The correlation between the morphological characteristics of these parasites and the paleobiogeographic data of their hosts enabled these authors to propose a phyletic tree for this group. The sub-order Trichostrongylina was divided into three super-families by Durette-Desset & Chabaud (1993): Trichostrongyloidea, Molineoidea and Heligmosomoidea. Remarkably, members of the three super-families are parasites of lagomorphs. From a phyletic point of view, lagomorphs played an evolutionary relay role between morphologically unchanged

hosts such as ratite birds or mammals that appeared in the early Eocene period, and more recent hosts, such as ruminants or arvicolin rodents (Durette-Desset & Chabaud, 1977, 1981; Mc Kenna & Bell, 1997).

The transfer amongst hosts lacking phyletic relationships is a general phenomenon in the nematode parasites of vertebrates and was defined by Chabaud (1965) as host-switching: a parasitic line may become isolated from its ancestral forms by passing from one host group to another; the isolation may be followed by evolutionary radiations of variable importance. In each super-family of the Trichostrongylina, host-switching may occur either at the time of the appearance and rapid diversification of a parasitic line which provides new ecological niches (for example the radiation of the Eutherian mammals at the beginning of the Tertiary) or between hosts having similar diets, such as the lagomorphs, ruminants and arvicolin rodents which are all herbivorous.

This classification is supported by biological data concerning these parasites. In strict herbivores, a derived life cycle appears with persistence of the sheathed infective larva, penetration of the host by the oral route only, and reduction of tissue migration. This recent life cycle contrasts with the life cycles of the majority of the Trichostrongylina, parasites of hosts which appeared during the Eocene period or which are not strict herbivores. These life cycles are charac-

* Département Systématique et Évolution, Muséum national d'Histoire naturelle, UMR 7138 associée au CNRS, BP 52, 61, rue Buffon, 75231 Paris Cedex 05, France.

** Laboratoire Informatique et Systématique, Université Pierre et Marie Curie, Paris 6, UMR 5143 associée au CNRS, 12, rue Cuvier, 75005 Paris, France.

Correspondence : Marie-Claude Durette-Desset.

E-mail : mcdd@mnhn.fr

	Parasite	Host	References	Parasite	Host	References
Trichostrongyloidea						
Trichostrongylidae						
Trichostrongylinae	<i>T. retortaeformis</i> (Zeder, 1800)	L	Michel, 1952a, b; Ford, 1971; Haupt, 1973; Barker & Ford, 1975; Audebert <i>et al.</i> , 2000, 2002a, 2003a	<i>T. axei</i> (Cobbold, 1879)	R	Douvres, 1957; Giordia & Bizzel, 1963; Ross <i>et al.</i> , 1967; Eysker, 1978, 1997
				<i>T. colubriformis</i> (Giles, 1952)	R	Mönning, 1927; Douvres, 1957; Bizzel & Giordia, 1965; Barker, 1975; Eysker, 1978; Rahman & Collins, 1990
				<i>T. rugatus</i> (Mönning, 1925)	R	Mönning, 1927; Beveridge & Barker, 1983; Barker & Beveridge, 1983
				<i>T. vitrinus</i> (Looss, 1905)	R	Dikmans & Andrews, 1933; Eysker, 1978; Taylor & Pearson, 1979; Rose & Small, 1984
Haemonchidae						
Ostertagiinae	<i>Graphidium strigosum</i> (Dujardin, 1845)	L	Wetzel & Enigk, 1937; Cabaret, 1981	<i>Ostertagia ostertagi</i> (Stiles, 1892)	R	Threlkeld, 1946; Douvres, 1956; Denham, 1969; Rose, 1969; Armour, 1970
				<i>Teladorsagia circumcincta</i> (Stadelmann, 1894)	R	Threlkeld, 1934; Sommerville, 1953a, b; Armour <i>et al.</i> , 1966
Haemonchinae				<i>Haemonchus contortus</i> (Rudolphi, 1803)	R	Veglia, 1916; Dikmans & Andrews, 1933; Keith, 1952; Silverman & Patterson, 1960
				<i>Haemonchus placei</i> (Place, 1893)	R	Bremner, 1956; Herlich <i>et al.</i> , 1958
Cooperiidae						
Libyostrongylinae	<i>Paralibyostrongylus hebrencuttus</i> (Lane 1923)	H	Cassone <i>et al.</i> , 1992	<i>Cooperia curticei</i> (Railliet, 1893)	R	Dikmans & Andrews, 1933; Andrews, 1939; Sommerville, 1960; Ahluwalia & Charlestone, 1974
Obeliscoidinae	<i>Obeliscoides cuniculi cuniculi</i> (Graybill, 1923)	L	Alicata, 1932; Sollod <i>et al.</i> , 1968	<i>Cooperia oncophora</i> (Railliet, 1898)	R	Dikmans & Andrews, 1933; Isenstein, 1963; Herlich, 1965b; Michel <i>et al.</i> , 1970; Amour <i>et al.</i> , 1987
	<i>O. cuniculi multistriatus</i> (Measures & Anderson, 1983)	L	Measures & Anderson, 1983; Watkins & Fernando, 1984, 1986	<i>Cooperia pectinata</i> (Ranson, 1907)	R	Herlich 1965a, b
Cooperiinae				<i>Cooperia punctata</i> (Linstow, 1907)	R	Ransom, 1920; Hung, 1926; Stewart, 1954; Bailey, 1949

Table I (to be continued).

	Parasite	Host	References	Parasite	Host	References
Molineoidea						
Nematodirinae	<i>Nematodiroides zembrae</i> Bernard, 1965	L	Audebert <i>et al.</i> , 2002b	<i>Nematodirus abnormalis</i> May, 1920	R	Onar, 1975; Beveridge <i>et al.</i> , 1985
				<i>Nematodirus battus</i> Crofton & Thomas, 1951	R	Thomas, 1957, 1959; Mapes & Coop, 1972
				<i>Nematodirus filicollis</i> (Rudolphi, 1802)	R	Boulenger, 1915; Thomas, 1957, 1959
				<i>Nematodirus belvetianus</i> May, 1920	R	Herlich, 1954
				<i>Nematodirus spathiger</i> (Railliet, 1896)	R	Kates & Turner, 1955; Thomas, 1957; Dineen <i>et al.</i> , 1965
Heligmosomoidea				<i>Heligmosomoides</i> <i>p. polygyrus</i> (Dujardin, 1845)	AR	N'Zobadila, 1994; N'Zobadila <i>et al.</i> , 1996a, b
<u>Heligmosomidae</u>	<i>Obbayashinema erbaevae</i> Durette-Desset, Ganzorig, Audebert, Kamiya, 2000	L	Audebert <i>et al.</i> , 2001	<i>Heligmosomoides p. bakeri</i> Durette-Desset, Forrester & Kinsella, 1972	AR	N'Zobadila, 1994; Cable <i>et al.</i> , 2006
				<i>Heligmosomoides laevis</i> (Dujardin, 1845)	AR	N'Zobadila, 1994; N'Zobadila <i>et al.</i> , 1996a
				<i>Heligmosomun mixtum</i> Schulz, 1954	AR	N'Zobadila, 1994; N'Zobadila <i>et al.</i> , 1996a

Abbreviations: H: Hystriidae, L: lagomorph, R: ruminant, AR: arvicolin rodent.

Table I. – Checklist of life cycles of Trichostrongylina, in natural hosts, lagomorphs, ruminants and arvicolin rodents. Classification of the Trichostrongyloidea after Durette-Desset *et al.*, 1999, classification of the Molineoidea and the Heligmosomoidea after Durette-Desset & Chabaud, 1981.

terized by an exsheathed infective larva, penetration by the cutaneous route, and pulmonary migration. The aim of this work was to confirm or refute the relay role of lagomorphs in the evolution of the Trichostrongylinae by summarizing previous works on the subject. Currently, 27 life cycles have been elucidated in natural hosts (lagomorphs, ruminant or arvicolin rodent), 16 in the Trichostrongyloidea, six in the Molineoidea and five in the Heligmosomoidea (Table I). 14 life cycles have been attempted in experimental hosts, eight in the Trichostrongyloidea, two in the Molineoidea, and four in the Heligmosomoidea (Table II). Also, a phylogenetic analysis was conducted, based on DNA sequence data to provide a suitable alternative to analyses based on morphological data and to examine the phylogenetic relationships of the three super-families within the Trichostrongylinae (Audebert *et al.*, 2005). The most important points treated in this study concern the chronology of the life cycles in the natural hosts, the parasitic phase in an experimental host and the adaptation involved, the migration of the parasite into the tissues of the host, the morphogenesis of the larval stages and molecular phylogeny.

MATERIALS AND METHODS

Hosts: in the Trichostrongyloidea and the Molineoidea, the experimental host is the rabbit (*Oryctolagus cuniculus*, Lilljeborg, 1874) (Lepo-

ridae) for the switch ruminant/lagomorph. The switch lagomorph/ruminant has never been attempted. In the Heligmosomoidea, the experimental host is the common vole (*Microtus arvalis*, Pallas, 1779) (Arvicolinae) for the switch lagomorph/ arvicolin rodent and the pica (*Ochotona rufescens rufescens*, Gray, 1842) (Ochotonidae) for the switch arvicolin rodent/lagomorph.

Parasites: the life cycles have been completed or attempted in the following families or sub-families: Trichostrongylinae, Haemonchinae, Cooperiinae (Trichostrongyloidea), Nematodirinae (Molineoidea) and Heligmosomidae (Heligmosomoidea) (see Table I).

Definitions: the prepatent period is divided into two periods: the "larval period" from the infestation of the host up to the appearance of the immature worm (moult 4) and the "maturation period" from the appearance of the immature worm to the presence of eggs in the faeces of the host (Audebert *et al.*, 2002a).

The fourth larval stage still sheathed in the cuticle of the third larval stage (or early L4) is designated as "(L4)" and the fourth larval stage exsheathed (or late L4) as "L4". DAI: day after the infestation.

Nomenclature and classification: the nomenclature used above the family group follows Durette-Desset & Chabaud (1993). The classification used for the Trichostrongyloidea follows Durette-Desset *et al.*, 1999 and that for the Molineoidea and the Heligmosomoidea Durette-Desset & Chabaud, 1981.

Parasite	Natural host	Experimental host	References
Trichostrongyloidea			
<i>Trichostrongylus colubriformis</i>	Cattle and other	Rabbit	Giordia <i>et al.</i> , 1966; Purvis & Sewell, 1971, 1972; Audebert <i>et al.</i> , 2003b
<i>Trichostrongylus vitrinus</i>	Cattle, sheep and goat	Rabbit	Audebert <i>et al.</i> , 2003b
<i>Trichostrongylus axei</i>	Cattle, sheep and deer	Rabbit	Drudge <i>et al.</i> , 1955; Leland & Drudge, 1957; Giordia <i>et al.</i> , 1966; Haupt & Nickel, 1975
<i>Cooperia curticei</i>	Sheep, goat, deer and mouflon	Rabbit	Wood & Hansen, 1960
<i>Cooperia punctata</i>	Cattle and various wild ruminants	Rabbit	Besh, 1964, 1965; Alicata, 1958
<i>Haemonchus contortus</i>	Sheep, goat, cattle, bison and deer	Rabbit	Wood & Hansen, 1960; Hutchinson & Slocombe, 1976; Mapes & Gallie, 1977
<i>Ostertagia ostertagi</i>	Cattle	Rabbit	Snider <i>et al.</i> , 1985, Boisvenue & Novilla, 1992
<i>Teladorsagia circumcincta</i>	Sheep, deer, llamas, mouflon, bighorn sheep and antelope	Rabbit	Zebrowska-Plata, 1980
Molineoidea			
<i>Nematodirus battus</i>	Sheep, goat and cattle	Rabbit	Gallie, 1972
<i>Nematodirus spathiger</i>	Sheep, goat and cattle	Rabbit	Audebert <i>et al.</i> , 2004
Heligmosomoidea			
<i>Obbayashinema erbaevae</i>	Ochoton	Field mouse	Audebert, 1999
<i>Heligmosomoides polygyrus polygyrus</i>	Field mice	Mouse	N'Zobadila, 1994
<i>Heligmosomoides polygyrus bakeri</i>	Mouse	Field mouse	N'Zobadila, 1994
<i>Heligmosomoides laevis</i>	Field mice	Ochoton	Audebert, 1999

Table II. – Checklist of studies concerning parasitic stages of parasites of lagomorphs, ruminants or arvicolin rodents in experimental hosts. Classification of the Trichostrongyloidea after Durette-Desset *et al.*, 1999, classification of the Molineoidea and the Heligmosomoidea after Durette-Desset & Chabaud, 1981.

SYNTHESIS OF THE DATA

CHRONOLOGY OF THE LIFE CYCLES IN NATURAL HOSTS

• Free phase

The duration of the free phase is from three to nine days in the Trichostrongyloidea, from eight to 30 days in the Molineoidea and from three to six days in the Heligmosomoidea (Table III).

• Parasitic phase

The duration of the larval period is from four to 15 days in the Trichostrongyloidea, from 10 to 15 in the Molineoidea and from four to seven in the Heligmosomoidea. The duration of the maturation period is from two to 16 in the Trichostrongyloidea, from two to 10 in the Molineoidea and from four to eight in the Heligmosomoidea. The duration of the prepatent period varies from 11 to 30 days in the Trichostrongyloidea,

from 14 to 21 days in the Molineoidea and from eight to 14 days in the Heligmosomoidea (Table III).

PARASITIC PHASE IN THE NATURAL HOST; COMPARISON BETWEEN THE LIFE CYCLES IN LAGOMORPHS AND THOSE IN RUMINANTS/ARVICOLIN RODENTS

In the Trichostrongyloidea, the larval period is shorter in lagomorphs than in ruminants or equivalent. The maturation period is shorter in lagomorphs. The prepatent period is shorter or equivalent in lagomorphs (Fig. 1A, B).

In the Molineoidea, the larval period is shorter in lagomorphs than in ruminants or equivalent and the maturation period is equivalent. The prepatent period is equivalent or longer in lagomorphs than in ruminants (Fig. 1C).

In the Heligmosomoidea the larval period and the maturation period are shorter in lagomorphs than in

Species	Host	Location	Morphogenesis	Free living stage	Parasitic stage			Prepatent period
			NIC of (L3)	Appearance of (L3) DAC	Moult 3 DAI	Moult 4 DAI	Arrested development	
Trichostrongyloidea				Free larva				
<i>Tr. retortaeformis</i>	L	intestine	16	5	3 & 5	4 & 6	(L4)	12 & 13
<i>Tr. colubriformis</i>	R	intestine	16	4	3 to 4	6 & 10	(L4)	18 & 21
<i>Tr. vitrinus</i>	R	intestine	16	3 to 5	4	11	L3	19
<i>Tr. axei</i>	R	intestine	16	4	4 to 6	10	L3	19
<i>Tr. rugatus</i>	R	intestine	16	3	4 to 6	10	absent	16 to 18
<i>G. strigosum</i>	L	stomach	16	3 to 5	2 to 9	11	L4	13
<i>Te. circumcincta</i>	R	stomach	16	4 to 6	3 to 4	8	L4	18
<i>H. contortus</i>	R	stomach	16	3	3	9 to 11	(L4)	11
<i>H. placei</i>	R	stomach	ud	ud	2	11 to 15	L4	24 & 30
<i>Os. ostertagi</i>	R	stomach	16	5 to 6	3	7 to 10	L4	23
<i>O. cuniculi cuniculi</i>	L	stomach	16	6	3 to 5	6 to 14	(L4)	16 to 20
<i>O. cuniculi multistriatus</i>	L	stomach	ud	7 to 8	3	8 to 11	(L4), L4	16 to 22
<i>C. curticei</i>	R	intestine	16	9	4	8 to 10	L4	15
<i>C. oncophora</i>	R	intestine	16	5	4	10	(L4)	17 to 22
<i>C. pectinata</i>	R	intestine	16	ud	3	8 to 10	L4	14 to 17
<i>C. punctata</i>	R	intestine	16	3 to 4	3	7 to 8	ud	12 to 16
Molineoidea				In shell				
<i>Nes. zembrae</i>	L	intestine	8	10 to 15	6	11	absent	21
<i>Nus. abnormalis</i>	R	intestine	8	16	4	12 to 14	(L4)	19
<i>Nus. battus</i>	R	intestine	8	28 to 30	4	10 to 12	L4 and Im	14
<i>Nus. filicollis</i>	R	intestine	8	24 to 27	5	12	L4 and Im	14 to 21
<i>Nus. belvetianus</i>	R	intestine	8	8 to 20	8	15	L4	21
<i>Nus. spatbiger</i>	R	intestine	8	14	5	11	L4	14
Heligmosomoidea				Free larva				
<i>Oh. erbaevae</i>	L	intestine	20	4 to 5	2.5	4	absent	8
<i>Hes. laevis</i>	AR	intestine	20	4	2.5	5	absent	9 to 12
<i>Hes. polygyrus polygyrus</i>	AR	intestine	20	6	3 to 4	5 to 7	absent	11
<i>Hes. polygyrus bakeri</i>	AR	intestine	20	6	4	6	absent	11
<i>Hum mixtum</i>	AR	intestine	20	3	2.5	6	absent	13 to 14

Abbreviations: *Tr.*: *Trichostrongylus*, *G.*: *Graphidium*, *Te.*: *Teladorsagia*, *H.*: *Haemonchus*, *Os.*: *Ostertagia*, *O.*: *Obeliscoidea*, *C.*: *Cooperia*, *Nes.*: *Nematodiroides*, *Nus.*: *Nematodirus*, *Ob.*: *Obbayasbinema*, *Hes.*: *Heligmosomoides*, *Hum.*: *Heligmosomum*. ud: unavailable data, NIC: number of intestinal cells, L: lagomorphs, R: ruminants, AR: arvicolin rodents, DAI: day after infestation, DAC: day after coproculture, L3: larva of stage 3, (L4): larva of stage 4 sheathed in L3 cuticle, L4: larva of stage 4, Im: immature worm; n° to n: same author, two data, n° & n°: different authors. In order to simplify the synthesis of data, the first date in the chronology for each species has been retained.

Table III. – Synthesis of data of life cycles of Trichostrongylina in natural hosts, lagomorphs, ruminants and arvicolin rodents.

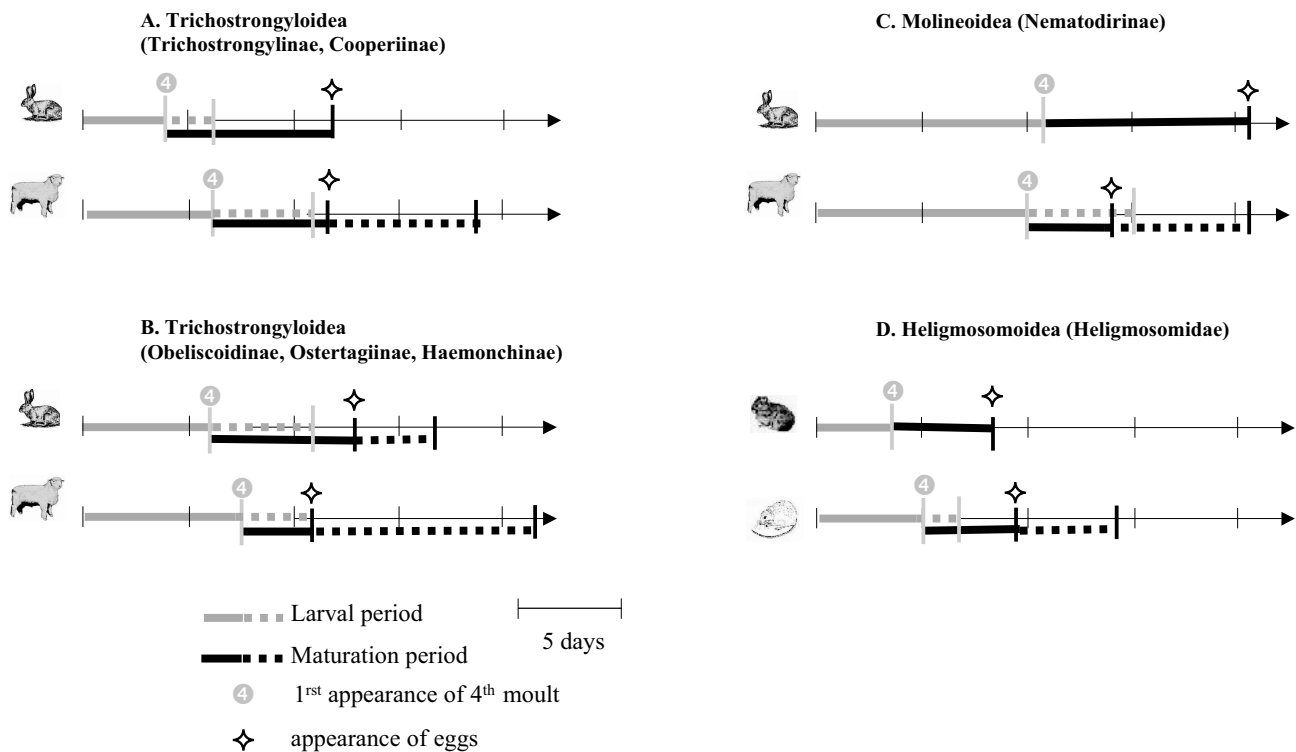


Fig. 1. – Chronology of parasitic life cycle in natural host; comparison between lagomorphs/ruminants and lagomorphs/arvicolin rodents. A: *Trichostrongylus retortaeformis* in rabbit and *T. axei*, *T. colubriformis*, *T. vitrinus*, *Cooperia curticei*, *C. oncophora*, *C. pectinata*, *C. punctata* in ruminants. B: *Obeliscoides cuniculi cuniculi*, *O. c. multistriatus*, *Graphidium strigosum* in rabbits and *Teladorsagia circumcincta*, *Haemonchus contortus*, *H. placei*, *Ostertagia ostertagi* in ruminants. C: *Nematodiroides zembrae* in rabbit and *Nematodirus abnormalis*, *N. battus*, *N. filicollis*, *N. helvetianus*, *N. spathiger* in ruminants. D: *Obbayashinema erbaevae* in ochoton and *Heligmosomoides laevis*, *H. polygyrus polygyrus*, *H. p. bakeri*, *Heligmosomum mixtum* in arvicolin rodents. The prepatent period is divided into “the larval period”, illustrated in light print and “the maturation period” in dark print. In the case of several species, the continuous line corresponds to the species with the shortest larval period and the shortest maturation period. The dotted line corresponds to the other species. In order to simplify the synthesis of data the first date in the chronology for each species has been retained. Scale: 5 days.

arvicolin rodents. The prepatent period is shorter in lagomorphs (Fig. 1D).

PARASITIC PHASE IN AN EXPERIMENTAL HOST;
COMPARISON BETWEEN THE LIFE CYCLE IN THE
NATURAL HOST AND IN THE EXPERIMENTAL HOST
(Table IV)

• Passage in experimental host

In the Trichostrongyloidea living in the small intestine (Trichostrongylinae, Cooperiinae) and in the Molineoidea (Nematodirinae), the life cycle can be completed and eggs are found in the faeces of the host (Fig. 2A, C).

In the Trichostrongyloidea living in the stomach (Ostertagiinae, Haemonchinae), the life cycle either stops at the L4 stage or else continues until the maturation of the adults but there is no presence of eggs in the faeces (Fig. 2B). In *Haemonchus contortus*, infestation by artificially exsheathed larvae results in recovery of only immature worms.

In the Heligmosomoidea (Heligmosomidae), there is no longer a host switch either from the ochoton to the

arvicolin rodent or from the arvicolin rodent to the ochoton (Fig. 2D).

• Duration of the prepatent period

In the Trichostrongyloidea, the prepatent period is shorter in the natural host. The larval period is shorter and the maturation period is shorter or equivalent (Fig. 2A, B).

In the Molineoidea, the prepatent period, the larval period and the maturation period are equivalent (Fig. 2C). In the Heligmosomoidea the comparison is not possible (Fig. 2D) because up to now it has been impossible to carry out a life cycle, the host switches arvicolin rodent/lagomorph and lagomorph/arvicolin rodent having been unsuccessful.

• Success rate of the infestation in experimental hosts

In the Trichostrongyloidea, the success rate of the switch ruminant/lagomorph is between 2.7 % and 23 % for the Trichostrongylinae (Table IV). In the Ostertagiinae, Cooperiinae and the Haemonchinae, the success rate is significantly lower between 0.01 % and 11 %.

Species	Experimental host	Success rate (%)	Parasitic stage			Comments
			Moult 3 DAI	Moult 4 DAI	Prepatent period	
Trichostrongyloidea						
<i>Tr. colubriformis</i>	rabbit	4.2 to 23	4	10	16	Eggs in faeces
<i>Tr. vitrinus</i>	rabbit	2.7 to 10.5	8	12	20	Eggs in faeces
<i>Tr. axei</i>	rabbit	18.6	8	14	22	Eggs in faeces
<i>C. curticei</i>	rabbit	2.5 to 6.25	ud	ud	18	A small proportion capable of development
<i>C. punctata</i>	rabbit	0.01 to 9.20	ud	ud	11-16	Mature worms are shorter than in calves
<i>H. contortus</i>	rabbit	0.3 to 11	5-7	9-12	No eggs	Artificially exsheathed, early L4, few immature worms
<i>Os. ostertagi</i>	rabbit	3.34	before 12	before 28	No eggs	Early L4 and immature worms
<i>Te. circumcincta</i>	rabbit	0.47 to 0.56	ud	10	No eggs	Many L4 and few immature with 4 th sheath
Molineoidea						
<i>Nus. battus</i>	rabbit	14.52	4	10	16	Some larvae L4 inhibited in development
<i>Nus. spatbiger</i>	rabbit	9.53	4	13	21	Some larvae L4 inhibited in development
Heligmosomoidea						
<i>Ob. erbaevae</i>	Arvicolin rodent	0	–	–	–	No development
<i>Hes. polygyrus polygyrus</i>	mouse	2.7	4-7	8	No eggs	Pseudocyst, expulsion of worms at 9 DAI
<i>Hes. polygyrus bakeri</i>	Arvicolin rodent	3.9	before 8	before 16	More 16	Asynchrony of moult
<i>Hes. laevis</i>	Ochotona	0	–	–	–	No development

Abbreviations: *Tr.*: *Trichostrongylus*, *C.*: *Cooperia*, *H.*: *Haemonchus*, *Os.*: *Ostertagia*, *Te.*: *Teladorsagia*, *Nus.*: *Nematodirus*, *Ob.*: *Obbayashinema*, *Hes.*: *Heligmosomoides*, DAI: day after infestation, L4: larva of stage 4, ud: unavailable data.

Table IV. – Synthesis of data concerning parasitic stages of Trichostrongylina in experimental hosts.

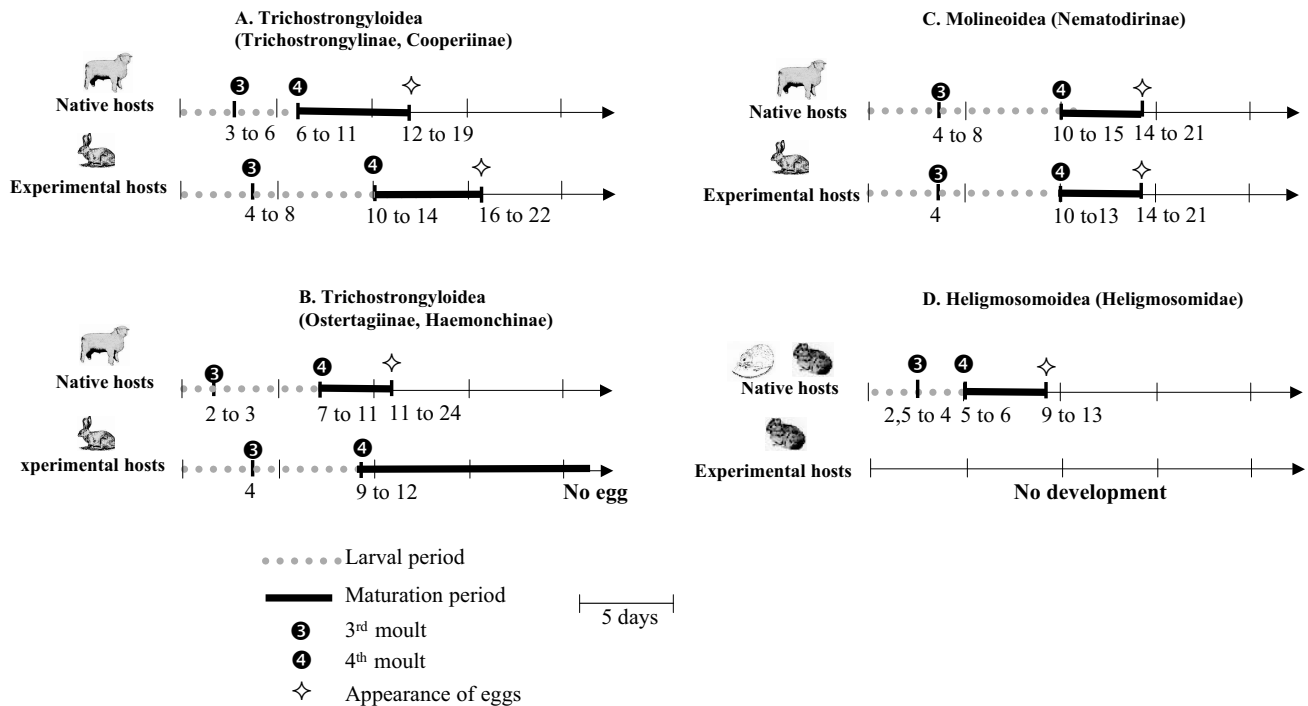


Fig. 2. – Chronology of parasitic life cycle; comparison between natural host and experimental host.

A: *Trichostrongylus axei*, *T. colubriformis*, *T. vitrinus*, *Cooperia curticei*, *C. oncophora*, *C. pectinata*, *C. punctata* in ruminants compared with *Trichostrongylus axei*, *T. colubriformis*, *T. vitrinus*, *Cooperia curticei*, *C. punctata* in experimental host, the rabbit. B: *Teladorsagia circumcincta*, *Haemonchus contortus*, *H. placei*, *Ostertagia ostertagi* in ruminants compared with *Teladorsagia circumcincta*, *Haemonchus contortus*, *Ostertagia ostertagi* in an experimental host, the rabbit. C: *Nematodirus abnormalis*, *N. battus*, *N. filicollis*, *N. helvetianus*, *N. spatbiger* in ruminants compared with *N. battus*, *N. spatbiger* in an experimental host, the rabbit. D: *Heligmosomoides laevis*, *H. polygyrus polygyrus*, *H. p. bakeri*, *Heligmosomum mixtum* in arvicolin rodents compared with *Heligmosomoides laevis* in an experimental host, the ochoton. Scale: 5 days.

In the Molineoidea (Nematodirinae), the success rate of the switch ruminant/lagomorph is between 9.5 % and 14.5 %.

In Heligmosomoidea, no success rate.

LOCATION OF LARVAL STAGES
IN THE DIGESTIVE MUCOSA AND ARRESTED DEVELOPMENT
(Tables I, III)

The data provided by the authors are heterogeneous and therefore difficult to compare. Nevertheless it is possible to group them by host and by super-family.

• Location of parasites

a. In lagomorphs

In the Trichostrongyloidea, the L3 penetrate the intramucosal capillaries (*Trichostrongylus retortaeformis*) (Audebert *et al.*, 2003a) or form ulcerations in the submucosa (*Obeliscoides* spp.) (Alicata, 1932). In the Molineoidea and the Heligmosomoidea, only the head is located in the mucosa (*Nematodiroides*, *Obbayashinema*) (Audebert *et al.*, 2001, 2002b).

b. In ruminants

In the intestinal Trichostrongyloidea (*Trichostrongylus* spp. and *Cooperia* spp.), and in Molineoidea, the L3 superficially penetrates the epithelium (Bailey, 1949; Kates & Turner, 1955; Herlich, 1965b; Barker, 1975; Taylor & Pearson, 1979; Barker & Beveridge, 1983; Armour *et al.*, 1987). In the gastric Trichostrongyloidea, the penetration is more superficial (*Haemonchus* spp.) (Silverman & Patterson, 1960) progressing to the formation of nodules in *Teladorsagia circumcincta* and *Ostertagia ostertagi* (Sommerville, 1953b; Armour, 1970)

c. In arvicolin rodent

In the Heligmosomoidea, the penetration is very deep resulting in the formation of pseudocysts located in the intestinal sub-mucosa, or musculosa or pedunculated in the abdominal cavity (N'Zobadila *et al.*, 1996b).

The duration inside the mucosa varies. Depending on the species of the parasite either the L4 or immature worms or adults reach the gastric or intestinal lumen, their definitive location, where coupling occurs.

• Arrested development

Arrested development is present in the Trichostrongyloidea and Molineoidea both in lagomorphs and ruminants. This phenomenon was the subject of a very detailed study of Michel (1974) and of various authors after him (Anderson *et al.*, 1965, Ogunsusi & Eysker, 1979; Watkins & Fernando, 1984, 1986; Gibbs, 1986; Eysker, 1978, 1997). The arrested development takes place at L3 or (L4) stage for *Trichostrongylus* spp., (L4) or L4 for the other genera. In the Molineoidea, it takes place at (L4) or L4 or immature stage.

In the Heligmosomoidea (Heligmosomidae), arrested development does not exist because pseudocysts empty

themselves and disappear from the beginning of the patent period (N'Zobadila *et al.*, 1996b).

MORPHOGENESIS (Fig. 3, Tables I, III)

Study of the larval morphogenesis during the life cycle of the Trichostrongyloidea highlights three significant points.

• Intestinal cell number of the free living stages

In each super-family, the number of intestinal cells of the free-living stage is constant. There are 16 in the Trichostrongyloidea (Veglia, 1916; Mönnig, 1927; Dikmans & Andrews, 1933; Douvres, 1957), eight in the Molineoidea (Nematodirinae) (Thomas, 1957; Audebert *et al.*, 2002b) and 20 in the Heligmosomoidea (Heligmosomidae) (N'Zobadila *et al.*; 1996a; Audebert *et al.*, 2001) (Table III).

• Shape of the tails of the larvae

In the Trichostrongyloidea, the tail of the free-living stages has a sharp tip and that of the L4 is rounded

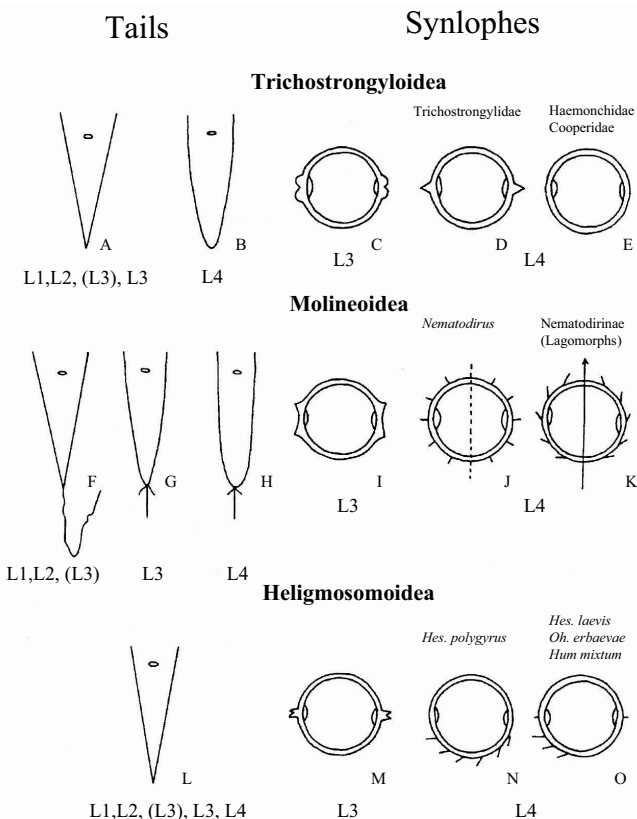


Fig. 3. – Morphological features of Trichostrongyloidea larvae during the ontogenesis; tails and synlophes.

A-E: Trichostrongyloidea, A-B: tails, C-E: transverse sections at midbody. F-K: Molineoidea, F-H: tails, I-K: transverse sections at midbody. L-O: Heligmosomoidea, L: tails, M-O: transverse sections at midbody.

Abbreviations: L1: larva of stage 1, L2: larva of stage 2, (L3): larva of stage 3 sheathed in L2 cuticle, L3: larva of stage 3, L4: larva of stage 4. Ob: *Obbayashinema*, Hes: *Heligmosomoides*, Hum: *Heligmosomum*.

(Fig. 3A, B), (Mönnig, 1927; Douvres, 1957; Audebert *et al.*, 2000). In the Molineoidea, the tails of L1, L2 and (L3) are whip-shaped (Fig. 3F). The tails of L3 and L4 are complex with several sharp tips, the longest being the median or the ventral (Fig. 3G, H) (Beveridge *et al.*, 1985; Audebert *et al.*, 2002b). In the Heligmosomoidea, the tails of L1 to L4 are simple and sharp (Fig. 3L) (N'Zobadila *et al.*, 1996a; Audebert *et al.*, 2001).

- Shape of the L3 lateral alae

In the Trichostrongyloidea, the L3 possesses small lateral alae, in the form of a double swelling (Fig. 3C) (Audebert *et al.*, 2000). In the Molineoidea, the L3 has two lateral alae made up of two triangular ridges well separated from each other (Fig. 3I) (Beveridge *et al.*, 1985; Audebert *et al.*, 2002b). In the Heligmosomoidea, the L3 has two lateral bifid alae (Fig. 3M) (N'Zobadila *et al.*, 1996a; Audebert *et al.*, 2001).

- Synlophe of the L4

In the Trichostrongyloidea, the synlophe of the L4 is absent in the Haemonchidae and the Cooperidae (Fig. 3E) or reduced to two triangular-shaped lateral alae, in species of the genus *Trichostrongylus*, parasites of lagomorphs or ruminants (Fig. 3D) (Audebert *et al.*, 2000). In the Molineoidea, the synlophe of both parasites of lagomorphs and ruminants presents a bilateral symmetry. In *Nematodirus* spp., a parasite of ruminants, the synlophe is made up of 10 cuticular ridges, orientated perpendicularly to the body surface (Fig. 3J) (Beveridge *et al.*, 1985); In *Rauschia* and *Nematodiroides*, both parasites of lagomorphs, it has an axis of orientation directed from the ventral to dorsal side (Fig. 3K) (Audebert *et al.*, 2002b). In the Heligmosomoidea, the synlophe never possesses a bilateral symmetry. In *Heligmosomoides polygyrus*, a parasite of rodents, it is made up of six small ventral ridges, orientated from right to left (Fig. 3N) (N'Zobadila *et al.*, 1996a). In the other Heligmosomidae studied, *Obbayashinema erbaevae*, a parasite of lagomorphs, and *Heligmosomoides laevis* and *Heligmosomum mixtum*, both parasites of rodents, there are three well developed ventral ridges and two tiny lateral ridges orientated perpendicularly to the body (Fig. 3O) (N'Zobadila *et al.*, 1996a; Audebert *et al.*, 2001).

MOLECULAR PHYLOGENY

Each super-family of Trichostrongylina represents a clade. Within the Trichostrongylina, the Trichostrongyloidea represents the sister group to a clade comprising the Heligmosomoidea and Molineoidea. These results were robustly sustained by high bootstrap and decay index values (see Audebert *et al.*, 2005). *Trichostrongylus retortaeformis* and *Graphidium strigosum*, parasites of lagomorphs are in the clade of the Tricho-

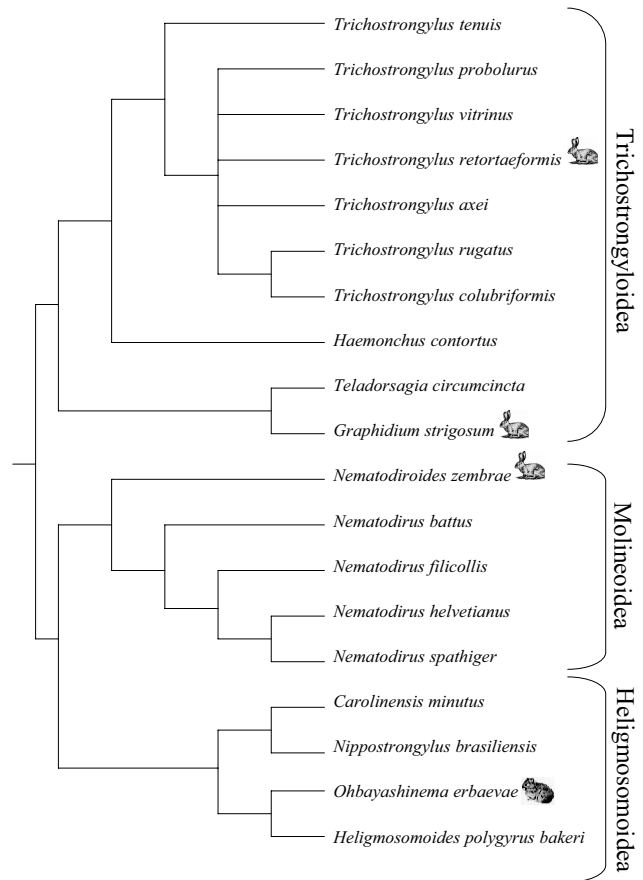


Fig. 4. – Cladogram depicting phylogenetic relationships of 19 species of nematodes within suborder Trichostrongylina, parasites of lagomorphs, ruminants and arvicolin rodents. The animal drawings next to the taxa show the parasites of lagomorphs. After Audebert *et al.*, 2005.

strongyloidea with the parasite of ruminants. *Nematodiroides zembrae*, a parasite of lagomorphs, is the sister group of *Nematodirus* spp., parasites of ruminants. *Obbayashinema erbaevae*, a parasite of ochotons, is in the clade of the Heligmosomidae parasites of the arvicolin rodents (Fig. 4).

INTERPRETATION OF DATA

CHRONOLOGY OF THE LIFE CYCLES IN NATURAL HOSTS

- Free phase

The duration of the free phase is similar in the Trichostrongyloidea and the Heligmosomoidea (3 to 9 days) whereas the duration is about one to four weeks in the Molineoidea. This difference could be explained by the fact that development occurs inside the egg in the Molineoidea.

- Parasitic phase

The duration of the life cycle may be correlated with the ecology of the hosts. The “r” strategy or “savannah”

type, is characterized by a fast reproductive cycle and a short life span, unlike the “k” strategy or “forest” type, characterized by a slow reproductive cycle and a long life span. The herbivorous hosts, which are studied in the present work, originate mainly from the savannah, which implies that their parasites also develop very quickly. Ochotons live in the mountains, not in the savannah. However the duration of the life cycle of their parasites is very short, like type “r” because ochotons experience a short warm season, which explains the rapid rhythm of reproduction of both host and parasite.

PARASITIC PHASE IN THE NATURAL HOST; COMPARISON BETWEEN THE LIFE CYCLES IN LAGOMORPHS AND THOSE IN RUMINANTS/ARVICOLIN RODENTS

The results are different for each of the three superfamilies: in the Trichostrongyloidea, the prepatent period is equivalent in lagomorph and ruminants; in the Molineoidea, the prepatent period is longer in lagomorphs than in ruminants, in the Heligmosomoidea, the prepatent period is shorter in lagomorphs than in arvicolin rodents.

PARASITIC PHASE IN AN EXPERIMENTAL HOST; COMPARISON BETWEEN THE CYCLE IN THE NATURAL HOST AND IN THE EXPERIMENTAL HOST: ADAPTATION TO THE EXPERIMENTAL HOST (Fig. 2)

In each case where the establishment of a parasite in an experimental host is still possible, the adaptation results in a lengthening of the larval period due mainly to the later appearance of moult 4, except for the Molineoidea where the duration of the larval period in the natural host and the experimental host do not change (Fig. 2).

One of the hypotheses put forward to explain the inability of the Haemonchidae to carry out their life cycle is that the acidity of the stomach of rabbits is insufficient to allow the development of the larvae. The rabbit is an abnormal host for ruminant parasites and since the digestive tract is very different from that of ruminants, it is conceivable that the normal growth pattern as well as the gross morphology of the worms may be influenced by various factors associated with this unusual habitat.

In the Heligmosomoidea, the life cycle in an experimental host is impossible and yet morphologically speaking, *Obbayashinema* and *Heligmosomoides* are very closely linked. This is in keeping with the observations of N'Zobadila (1994) even those concerning the genus *Heligmosomoides* itself. This author carried out cross infestations between *H. p. bakeri* Durette-Desset *et al.*, 1992, a parasite of the domestic mouse in the USA and *H. p. polygyrus* (Dujardin, 1845) a parasite of *Apodemus sylvaticus* in Europe. In experimental condi-

tions, the life cycle of *H. p. polygyrus* in the mouse cannot proceed beyond the appearance of the juvenile worms and the adult worms are expelled 9 DAI. The life cycle of *H. p. bakeri* in *Apodemus*, by contrast, develops a longer maturation period. At 16 DAI, the end of the experiment, the worms are still at the immature stage. Moreover, the rate of establishment for both species is very low, 3 and 4 %, respectively. In this group, the biological features concerning parasitic specificity thus appear more marked than the morphological features. This biological observation was recently confirmed by molecular data in Cable *et al.*, 2006.

LOCATION OF LARVAL STAGES IN THE DIGESTIVE MUCOSA AND ARRESTED DEVELOPMENT (Tables I, III)

According to Chabaud (1955), the life cycle of primitive Strongylida (*Ancylostoma* type), begins with cutaneous penetration of exsheathed infective larvae, followed by the migration of larvae via the circulatory or lymphatic system to the lungs. The larvae are subsequently coughed up and swallowed, thus arriving at their definitive site, the intestine. The Trichostrongylina, which are parasites of hosts whose diet is herbivorous, such as lagomorphs, ruminants and arvicolin rodents, have a completely different life cycle with penetration of sheathed infective larvae by the oral route and the absence of pulmonary migration. However, the intra-tissular maturation present in the larval stages of the primitive life cycles, is replaced in these parasites, by penetration of the larvae into the gastric or intestinal mucosa. This penetration is either superficial or deep, depending on the genus of the parasite. (Table D). This phenomenon highlights the fact that an intra-tissular phase is essential to larval development.

This mucosal maturation seems to have given rise to acute adaptation in some life cycles because larvae in the mucosa can temporarily arrest their development. This may be interpreted as an adaptative phenomenon in order to limit the number of parasites present (massive or repetitive infestations) or to preserve the parasite when conditions are unfavourable in the natural environment, *i.e.* seasonal influences on infective larvae on pasture (Levine, 1963; Eysker, 1997; O'Connor *et al.*, 2006) or the host immune responses can inhibit the normal development of the parasitic phase of the life cycle (Eysker, 1978, Christensen *et al.*, 1992).

In the Heligmosomidae, this arrest of development does not exist since the larvae leave the pseudocyst which disappears at the beginning of the patent period. In this case the pseudocysts may represent the final stage needed for larval maturation (N'Zobadila *et al.*, 1996b).

MORPHOGENESIS

In the current classification mainly based on the morphology of the adults, the Trichostrongylina parasites of lagomorphs are present in all three super-families (Durette-Desset, 1985). In each super-family, the parasites of lagomorphs are present in the same sub-family (or genus for *Trichostrongylus*) as those of ruminants (Trichostrongyloidea, Molineoidea) or in the same family (Heligmosomoidea). Morphogenesis pertaining to the ontogenesis of three morphological characters strongly confirmed this classification.

- Intestinal cell number of the free living stage

The differences observed between the three super-families appear to be correlated to two different larval strategies. In the Trichostrongyloidea and the Heligmosomoidea, the eggs hatch early, the free-living stages and nutrition occurring in the external environment. The development takes place within four to six days in the Trichostrongyloidea (16 intestinal cells) and within three to six days in the Heligmosomoidea (20 intestinal cells). In the Molineoidea (Nematodirinae) the strategy is different; the “free” living stages occur in the egg at the expense of the vitelline reserves but with a low risk of predation, which results in a slow development from 10 to 28 days and only eight intestinal cells.

- Shape of the tails of the larvae

A larval feature, the shape of the tails (L1 to L4), is characteristic of two host groups (lagomorphs/ruminants or lagomorphs/arvicolin rodents) in each of the three super-families (Fig. 3).

- Shape of the L3 alae and synlophe of L4

In L3, the shape of lateral alae is different for the three super-families, but similar within one super-family for both host groups. The synlophe of the adult is an essential character defining the three super-families. In L4, this synlophe is already pre-established as in the adult: absent in the Trichostrongyloidea, with bilateral symmetry in the Molineoidea, without bilateral symmetry in the Heligmosomoidea. This represents additional proof of the systematic value of the synlophe.

MOLECULAR PHYLOGENY

The phylogenetic tree of the parasites corresponds to the classification proposed by Durette-Desset (1985) and Durette-Desset *et al.* (1999): in each super-family the parasites of lagomorphs/ruminants or lagomorphs/arvicolin rodents are monophyletic. Elsewhere, it has been demonstrated that each host group is monophyletic (for lagomorphs and rodents see Lockett & Hartenberger (1993) and Chaline *et al.* (1999); for ruminants see Hernandez & Vrba (2005)). The superposition of the two trees indicates that neither the parasites of

lagomorphs nor the parasites of ruminants or arvicolin rodents constitute a monophyletic group (Audebert *et al.*, 2005).

CONCLUSION

In the studies concerning the phylogeny of the Trichostrongylina (Durette-Desset & Chabaud, 1977, 1981, Durette-Desset, 1985; Durette-Desset *et al.*, 1999) the following hypothesis has been constantly developed.

The whole of ancestral Trichostrongylina has been expanded in vertebrates such as amphibians, reptiles, rats, other birds and in “ancient” mammals such as marsupials, Insectivora, Chiroptera and some rodents. Those hosts appeared before or during the Eocene period. While not belonging to the same phyletic line, they shared the same pattern of life cycle with a cutaneous penetration and a pulmonary migration before reaching the definitive location in the host (gastric or intestinal). By contrast, the life cycles of the parasites of lagomorphs are completely different because infestation occurs by the oral route and tissular migration is reduced. In the current fauna, the majority of parasite species of ruminants which, according to the previous hypothesis originate from parasites of lagomorphs, presents this same type of life cycle (Durette-Desset *et al.*, 1999, Hoberg *et al.*, 2005).

The transition between the two types of life cycle has been brought to the fore in the genus *Paralibyostrongylus*, Ortlepp, 1939. From the previous hypothesis, this genus is particularly interesting because it parasitises both “ancient” vertebrates and lagomorphs. The life cycle of *Paralibyostrongylus hebreanicus* (Lane, 1923), a parasite of *Atherurus*, was described by Cassone *et al.* (1992) in this natural model, and also in the guinea pig and the rabbit. However, *Paralibyostrongylus* spp. is also present, in wild Leporidae. In the classification of Durette-Desset *et al.*, 1999, the genus was situated at the base of the Cooperidae (Libyostrongylinae-Cooperiinae). Cassone *et al.*, 1992, showed that there are two transmission routes, which may have made possible the transition from the primitive cycle by cutaneous penetration to the more specialized cycle by the oral route, the latter being responsible for the evolutionary success of the group in large herbivores.

The lagomorphs appear to have a relay role regardless of the parasitic group. The lagomorphs appeared at the upper Eocene period in the Nearctic zone. They were present in Europe and in Asia at the lower Oligocene period and reached Africa in the lower Miocene period.

The contamination of ruminants and arvicolin rodents by the Trichostrongyloidea apparently took place after

that of the lagomorphs. Later, the switch occurred from many species (Durette-Desset, 1985; Durette-Desset *et al.*, 1999).

Trichostrongyloidea: in the Trichostrongylidae within the genus *Trichostrongylus* itself, in the Haemonchidae, from *Graphidium* and *Hyostrongylus*, in the Cooperiidae, from *Paralibyostrongylus* and *Obeliscoides* (Durette-Desset *et al.*, 1999).

Molineoidea: in the Nematodirinae from a common ancestor to *Rauschia* (Durette-Desset, 1979) and *Nematodirus* (Rossi, 1983; Hoberg *et al.*, 2005).

Heligmosomoidea: in the Heligmosomidae, from *Obbayashinema* (Durette-Desset *et al.*, 2000).

The aim of this study was to determine if morphogenesis, biological and molecular data were opposed to the previous hypotheses, based only on morphological data of the parasites and on paleobiogeographical data of the hosts. All the summarized data (chronology of life cycle, adaptation to the experimental host, tissular migration, morphogenesis; molecular phylogeny) are in agreement with the previous hypothesis. These data confirm that the lagomorphs may be considered as “relay” hosts in the evolution of the Trichostrongylina.

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