The evolutionary ecology of host-specificity: experimental studies with *Strongyloides ratti*

A. W. GEMMILL[1], M. E. VINEY[2] *and* A. F. READ[1]*

[1] *Institute of Cell, Animal and Population Biology, University of Edinburgh, West Mains Road, Edinburgh EH9 3JT, UK*
[2] *School of Biological Sciences, University of Bristol, Woodland Road, Bristol BS8 1UG, UK*

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SUMMARY

Factors constraining the evolution of host-specificity were investigated using a gastrointestinal parasitic nematode, *Strongyloides ratti*. *S. ratti* is a natural parasite of rats which can also reproduce, with decreased success, in laboratory mice. Observed host-specificity arose from lower establishment, reduced *per capita* fecundity and more rapid expulsion of parasites from mice relative to rats. Variation in the efficacy of thymus-dependent immunity between host species (rats and mice) was insufficient to explain the majority of the observed differences in parasite establishment and reproductive success. The role of natural selection in determining host-specificity was addressed using experimental selection followed by reciprocal fitness assays in both host species. Experimental selection failed to modify the host-specificity of *S. ratti* to any measurable degree, suggesting either a lack of genetic variation for this trait or the involvement of as yet unidentified factors underlying the differences in *S. ratti* fitness in rats and mice respectively. These results are discussed in relation to competing theoretical models of ecological specialization, host immunology and previous attempts to experimentally alter the host-specificity of parasitic nematodes

Key words: host-specificity, specialization, nematodes, *Strongyloides ratti*, evolution.

INTRODUCTION

Uncovering the causes of host-specificity is a key issue in parasitology (Rohde, 1994). Why are some parasites found in only one host species, whereas others are found in 2 or more? Why do no parasite species infect all the species in large clades such as birds or mammals? These questions illustrate a central problem in evolutionary ecology (Futuyma & Moreno, 1998; Thompson, 1994): when does natural selection favour the evolution of specialists over generalists? In parasitology, this is not only of theoretical interest. Understanding what limits host range may prove valuable in designing successful parasite control measures. Concern over newly emerging diseases, many of which are zoonotic in origin (Murphy, 1998), underlines the need for answers to these questions.

Despite this, our understanding of host-specificity remains rudimentary. As Begon, Harper & Townsend (1996) (p. 440) pointed out: '... we assume that the existence of a narrow and restricted range of hosts ... represents some sort of evolutionarily optimal condition. We presume that natural enemies, chemical defences or some other force would reduce the fitness of any parasites that extended the range. These are rash assumptions that beg to be tested.'

Strongyloides ratti is a natural parasite of rats (*Rattus norvegicus*) but can also complete its life-cycle (with reduced success) in laboratory mice (*Mus musculus*) (Dawkins *et al.* 1980; Ovington *et al.* 1998). *S. ratti* infections are common in wild rats (Wertheim & Lengy, 1964; Fisher & Viney, 1998). Yet, so far as we know, there have only been 2 reports since the late nineteenth century of *Strongyloides* spp. in wild-caught mice (Grassi & Serge, 1887; Prokopic & Del Valle, 1996), one of which classified the species as *S. ratti* (Prokopic & Del Valle, 1966). The absolute non-dispersal of *Strongyloides* to wild mice therefore seems unlikely. But these records are exceptions, even though wild mice are frequently sampled by parasitologists, and members of the genus *Strongyloides* routinely turn up in parasitological surveys of other hosts. What prevents *S. ratti* from expanding its host range?

Answers to this sort of question can be sought at a number of levels. First, which components of parasite fitness are altered in novel hosts – establishment, adult survivorship, or fecundity? Second, what factors mediate these changes? Host defences are a major cause of fitness reductions in natural host–parasite combinations. Is overcoming these defences the major hurdle preventing expansion of host range or are differences in morphology, physiology and biochemistry among host species more important? Third, why has natural selection not

* Corresponding author: Institute of Cell, Animal and Population Biology, University of Edinburgh, West Mains Road, Edinburgh EH9 3JT. Tel: +44 131 650 5506. Fax: +44 131 667 3210. E-mail: a.read@ed.ac.uk

produced more species of generalist parasite? The role of host-specific adaptation (specialization) in determining observed levels of host-specificity is likely to be substantial, but is more often inferred than demonstrated directly (Second & Kareiva, 1996; Tompkins & Clayton, 1999).

Currently, 2 broad classes of explanation exist for the evolution of ecological specialization – models based on trade-offs and models based on habitat-specific selection (Templeton & Rothman, 1974; Via & Lande, 1985; Futuyma & Moreno, 1988; Kawecki, 1998). The former assume that adaptation to one environment reduces an organism's ability to exploit other environments. Such trade-off models require that negative genetic correlations exist between habitat-specific fitness components. However, these negative correlations have been rarely found (Rausher, 1988; Via, 1990; Fry, 1996; Whitlock, 1996, but see Mackenzie, 1996). Recent models ignore trade-offs and consider the effects of population subdivision in driving the evolution of specialization (Kawecki, 1996, 1997, 1998; Whitlock, 1996). In these models adaptation to a particular habitat (fixation of alleles whose beneficial effects are habitat specific) is both more probable and more rapid in populations confined to that habitat than in populations that are spread between several environments. This is because a higher proportion of gene copies with habitat-specific effects are exposed to selection in habitat-restricted populations – the more environments a population inhabits, the weaker the strength of selection on loci with effects specific to each of those environments. Similarly, populations which are spread across several environments carry higher habitat-specific mutation and drift loads (the accumulation of deleterious alleles with habitat-specific effects is more likely) resulting in lowered average fitness of those populations (Whitlock, 1996; Kawecki, 1997).

Here, we report attempts to address the mechanistic and evolutionary basis of host specificity in *S. ratti* by experiment. We first quantify the differences in infection kinetics between rats and mice which are immediately responsible for host-specificity. Second, we evaluate the role of a proximate biological mechanism capable of generating these differences, namely the thymus-dependent (T-dependent) vertebrate immune system, by making use of congenitally athymic rats and mice. T-dependent lymphocyte activation and proliferation play a major role in the control of most parasitic nematode infections (Maizels *et al*. 1993; Maizels & Holland, 1998). In both *R. norvegicus* and *M. musculus*, single recessive mutations exist (*nude* or *nu*) which in the homozygous state result in the absence of a functional thymus. Homozygous *nu* individuals are thus incapable of mounting effective T-dependent immune responses, typically resulting in exacerbation and/or prolongation of experimental infections (e.g. Dawkins, Mitchell & Grove, 1982; Gemmill, Viney & Read, 1997). Finally, we employ experimental selection and reciprocal cross-infections of an isofemale line of *S. ratti* to assess how quickly and in what direction natural selection might act to change host-specificity. If selection leading to increased fitness in one host involves a contemporaneous decrease in fitness in another, a negative genetic correlation (trade-off) is implicated in maintaining host-specificity. In contrast, if adaptation to one host is accompanied by a negligible or delayed decrease in fitness on another, this suggests mutations and drift due to relaxed selection on loci with host-specific effects as possible causes of host specificity

MATERIALS AND METHODS

Parasites and parasitology

Adult females of *S. ratti* are parthenogenetic and inhabit the host small intestine (Viney, 1994). Eggs are shed into the intestine and pass out with host faeces. These offspring then develop in the external environment. The isofemale *S. ratti* line ED5 Homogonic (Viney, 1996) was used in all experiments and was maintained by serial passage in female Wistar rats (Banton and Kingman, UK). Food and water were provided to animals *ad libitum*. Unless otherwise stated, experimental infections were initiated by subcutaneous injection of inocula containing 500 infective 3rd-stage larvae (iL3s) suspended in physiological saline (0·8 % (w/v) NaCl solution). Inocula were prepared by serial dilution from a worm-containing suspension of known volume. For assessment of parasite reproductive output (worm output), faeces were collected overnight and divided equally between 2 culture plates (mice) or 3 culture plates (rats). Cultures were prepared as described by Viney, Matthews & Walliker (1992) and incubated for 2 days at 25 °C. Infective 3rd-stage larvae were then washed from culture plates, collected and counted under a binocular microscope as described elsewhere (Gemmill *et al*. 1997).

Numbers of intestinal parasites (worm burdens) were determined as follows. The small intestine between stomach and caecum was excised, opened longitudinally and rinsed briefly in tap water to remove excess digesta. These initial rinses were subsequently checked for the presence of parasites with none being found on any occasion. Each small intestine was then divided into 3 approximately equal parts and each part incubated separately in gradated 50 ml conical tubes (Corning, USA) containing approximately 25 ml of physiological saline. After incubation for 2 h at 37 °C, each portion of small intestine was vigorously rinsed and backwashed with fresh physiological saline in order to detach any remaining parasites. Parasites from each individual animal were then concentrated into a

single suspension and counted under a binocular microscope.

To check that this method generates unbiased estimates of worm burdens, the following experiment was conducted. Six Wistar rats and 6 C57 mice were each infected with 500 iL3s as described above. All were killed on day 5 post-infection (p.i.), and worms in the gastrointestinal tracts of 3 mice and 3 rats were estimated exactly as above. The gastrointestinal tracts of the other 6 hosts were slit longitudinally, squashed between glass plates, and examined for adult worms under a binocular microscope. Estimates of worm burdens obtained by the 2 methods did not differ significantly (mean worm burdens ± 1 S.E.M.: mouse, $22 \pm 3{\cdot}2$ and $24 \pm 7{\cdot}4$; rat, $203 \pm 43{\cdot}8$ and $155 \pm 26{\cdot}3$ for the incubation and squash methods respectively; two-way ANOVA, main effect of method: $F_{1,8} = 0{\cdot}79$, $P = 0{\cdot}39$, interaction of method and host species: $F_{1,8} = 0{\cdot}94$, $P = 0{\cdot}36$). Thus, incubation for 2 h at 37 °C is sufficient for the adult worms to free themselves from the mucosa.

Throughout the study, the order in which experimental animals were infected, the positions of cages in which faecal pellets were collected, the order in which intestinal contents and cultures were processed and counted, as well as the positions of cultures in incubators, were randomized anew at each sampling point using random numbers generated by the Excel 5.0 software package.

Establishment and expulsion

To determine the kinetics of parasite establishment in, and expulsion from, the small intestine, the following experiment was conducted. Experimental animals were 6-week-old male Wistar rats and male C57/BL/6J mice (B & K, UK). Worm burdens were determined in groups of 5 rats and 5 mice sacrificed on days 4, 5, 7, 9, 11 and 14 p.i. Faeces from the animals killed on day 14 p.i. were collected overnight prior to each day of sacrifice, cultured and worm outputs determined as detailed above. This design also allowed an estimate of *per capita* fecundities (offspring per parasite per night), calculated by dividing mean nightly worm output by worm burden determined the following morning

Thymus-dependent immunity

To determine whether T-dependent immunity is involved in the different performance of *S. ratti* in rats and mice, an experiment was conducted using congenitally athymic and wild type host animals. Six homozygous *nude* mice (BALB/cOlaHsd-*nu*/*nu*) and 6 heterozygous mice (BALB/cOlaHsd-*nu*/+), along with 6 homozygous *nude* rats (Hsd:RH-*rnu*/*rnu*) and 6 heterozygous rats (Hsd:RH-*rnu*/+) were infected with ED5 Homogonic. All animals were 6-week-old males (Harlan, UK). To prevent bacterial infections, all 24 animals (homozygous and heterozygous rats and mice) received a wide-spectrum antibiotic (Baytril, Bayer) at a concentration of 0·01 % (w/v) in drinking water. Worm output was monitored from day 4 p.i. until day 33 p.i.

Selection experiment

Some strains of *M. musculus* are almost entirely refractory to infection with *S. ratti* (Dawkins *et al.* 1980). Therefore, prior to the start of the selection experiment, 4 commercially available mouse strains – MF-1, C57/BL/6J, TO and ICR (B & K, UK) – were assessed for resistance to *S. ratti* (data not shown). Only from the C57/BL/6J strain was worm output sufficient to ensure continuing inoculum sizes of around 500 individuals.

The design of the selection experiment is shown in Fig. 1. At each generation host animals were age-matched male Wistar rats (B & K, UK) and male C57/BL/6J mice (from a colony maintained at the University of Edinburgh or from Harlan, UK) 6–7 weeks old. Five lines were established and maintained independently in a single rat at each generation (lines R1–R5). A further 5 lines were maintained separately in pairs of mice (lines M1–M5). Mice were infected in pairs to ensure sufficient parasite offspring for subsequent generations. Faeces collected from both mice within each line were pooled. Infections which initiated each line were designated as generation zero (G0). On each infection day, each animal in the experiment (rat or mouse) was infected with 500 iL3s collected from the previous generation of the relevant worm line. Here, a generation is defined as a cohort of parasitic females. If, at any generation, a selected line failed to produce sufficient viable iL3s, inocula sizes in all selected lines were reduced to the number available in the line with the fewest viable worms. On day 5 p.i., faeces were collected overnight from pairs of mice or from single rats, cultured and incubated for 2 days at 25 °C. Infective 3rd-stage larvae were then washed from culture plates and the number present in each set of plates determined. From each line, an arbitrary sample of these worms, collected on day 5 p.i., was chosen to parent the next generation. In this experimental design, parents are not selected on the basis of their individual phenotypic trait values: all iL3s collected from culture plates on the day of infection have an approximately equal probability of being chosen. Thus, no artificial selection is operating (Falconer & Mackay, 1996). Any response to selection must result from the action of natural selection alone

Reciprocal infection

To assess the effects of selection in one host on the fitness of selected parasites in that or the other host

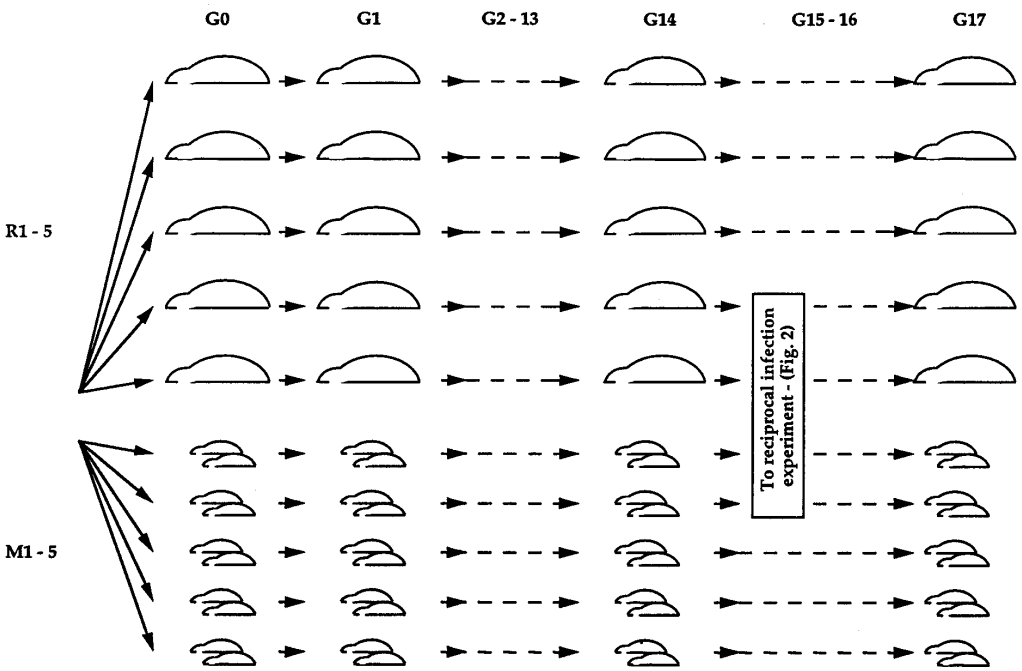

Fig. 1. Design of the selection experiment. Worms from a single isofemale line of *Strongyloides ratti* were used to initiate 5 worm lines passaged in naive rats (R1–5) and 5 in naive mice (M1–5). Each of the mouse lines was run through 2 mice (see text for further details). G (generation) refers to the passage number. After 14 generations, worms from 4 randomly chosen lines, 2 from each host species, were used in the reciprocal infection experiment (Fig. 2), but all 10 selection lines were maintained for another 4 generations before the experiment was terminated. Large symbols, rats; small symbols, mice.

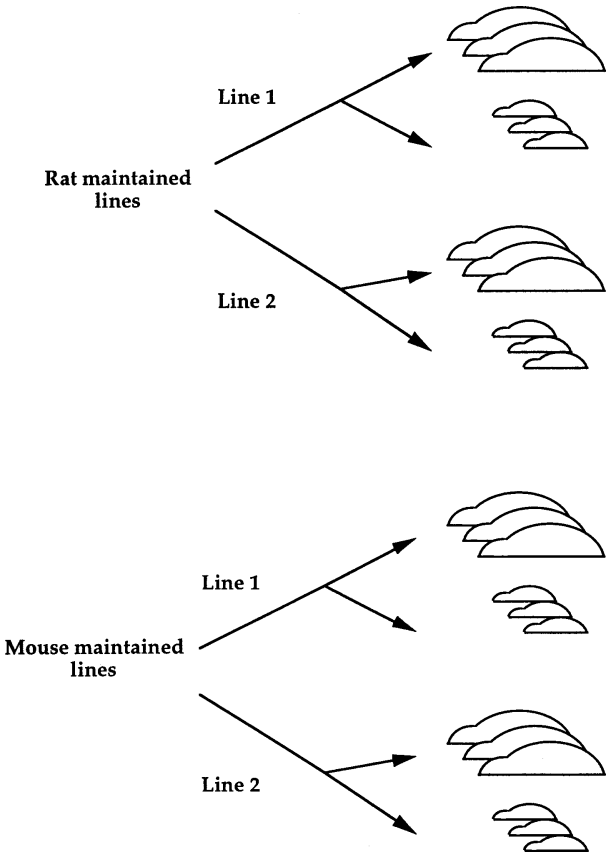

Fig. 2. Design of the reciprocal infection experiment. The fitness of 2 of each of the rat- and mouse-maintained lines (Fig. 1), chosen at random, was compared in 3 rats and 3 mice. See text for details. Large symbols, rats; small symbols, mice.

species, a reciprocal cross-infection design was employed (Fig. 2). For practical reasons, not all selected lines could be assayed in both host species simultaneously. At G14, two of lines R1 to R5 and two of lines M1 to M5 were chosen randomly. For each line thus chosen, infections were initiated and worm output assayed in both rats and mice ($n = 3$ animals per host species per selected line) on days 5, 8 and 11 p.i.

Statistical analysis

The total number of parasite offspring produced during an infection (total worm output) was estimated by numerical integration of the area under the nightly worm output by day p.i. curves. Where necessary, data were $\log_{10}$ transformed ($\log_{10}$ [value + 1]) prior to analysis. One-factor, two-factor and repeated measures ANOVAs were carried out in the Statview 4.5 program. Where faeces were collected from pairs of mice (the selection experiment), numerical values of nightly worm outputs were halved for the purposes of graphical presentation

RESULTS

Relative success of S. ratti *in rats and mice*

Nightly worm output from animals sacrificed for worm burden counts on day 14 p.i. are shown in Fig. 3. Parasite offspring were first detected in the faeces

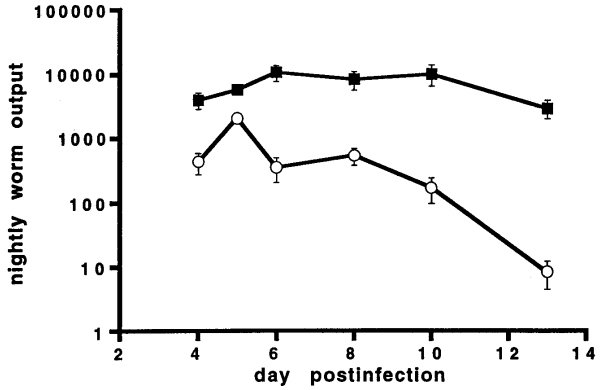

Fig. 3. Reproductive success of *Strongyloides ratti* in rats (■: $n = 5$ rats) and mice (○: $n = 5$ mice). Plotted values are mean nightly worm outputs (± 1 S.E.M.) per host animal. In some cases, error bars are smaller than symbol.

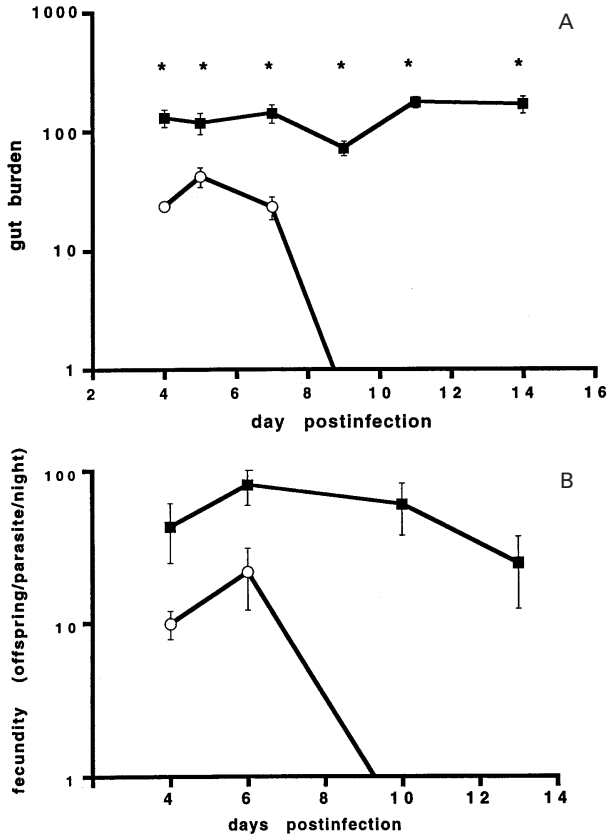

Fig. 4. Kinetics of (A) worm burdens and (B) *per capita* parasite fecundity in rats (■: $n = 5$ rats at each data point) and mice (○: $n = 5$ mice at each data point). Plotted values are (A) mean worm burdens and (B) estimated mean egg output per female per night. Asterisks denote significant differences ($P < 0{\cdot}0083$, see text) between rats and mice as assessed by ANOVA on $\log_{10}$ transformed values. In both (A) and (B), error bars are ± 1 S.E.M. In some cases, error bars are smaller than symbol.

of all animals on day 4 p.i. Mean worm output from rats on day 5 p.i. was about 3 times greater than that from mice (Fig. 3: $F_{1,8} = 22$, $P < 0{\cdot}01$). A repeated-measures ANOVA with day p.i. fitted as a within-subject factor and host species fitted as a between-subject factor (where subjects are host individuals), revealed that the pattern of worm output through time differed between the 2 host species (interaction of host species with day p.i.: $F_{5,40} = 3{\cdot}17$, $P < 0{\cdot}05$; main effects: host species, $F_{1,40} = 17{\cdot}16$, $P < 0{\cdot}01$; day p.i., $F_{5,40} = 2{\cdot}9$, $P < 0{\cdot}05$). Output in rats remained high throughout sampling but was barely detectable in mice by day 13 p.i. Total worm output up to day 14 p.i. was 16 times greater in rats than in mice ($F_{1,8} = 72$, $P < 0{\cdot}0001$). Thus, *S. ratti* established and reproduced in C57/BL/6J mice, but reproductive success was substantially less than that achieved in rats.

Establishment, expulsion and fecundity

Intestinal worm burden kinetics in rats and mice paralleled the nightly worm output curves. Since there are 6 separate sampling points to analyse and because multiple statistical tests can yield significant results by chance alone, we first used the standard Bonferroni correction technique (Rice, 1989) to establish the appropriate significance level to apply to each test ($0{\cdot}05/6 = 0{\cdot}0083$). Worm burdens were significantly higher in rats compared to mice at every point (Fig. 4A). There was a 5-fold difference in peak worm burden between rats (peak at day 11 p.i.) and mice (peak at day 5 p.i.) ($F_{1,8} = 36$, $P < 0{\cdot}001$). All parasites were expelled from the intestines of mice by day 14 p.i., while worm burdens in rats remained high. *Per capita* parasite fecundity estimates were significantly different between rats and mice, being 4–5 times greater in rats on the day of peak egg production (Fig. 4B; day 6 p.i.: $F_{1,8} = 6{\cdot}46$, $P < 0{\cdot}05$). Thus, both establishment rates and the life-time reproductive success of established worms were reduced in mice by a similar magnitude.

The role of thymus-dependent immunity

Nightly worm outputs from nude and normal rats and mice are shown in Fig. 5A. Worms were detected in the faeces of all nude and normal rats, and normal mice, on day 4 p.i. Only 1 nude mouse had a patent infection at this time, the remaining 5 nude mice produced no worms until day 5 p.i. Worm outputs from nude animals of both species remained elevated for a prolonged period compared to that from normal, conspecific animals. Although this led to a more than 6-fold difference in total worm output between nude and normal rats (Fig. 5B: $F_{1,10} = 48$, $P < 0{\cdot}0001$), nude mice did not produce significantly more worms than did normal mice ($F_{1,10} = 2{\cdot}1$, N.S.). Thus, thymic status affected total worm output differently in rats and mice respectively (interaction of host species with thymic status: $F_{1,20} = 6{\cdot}1$,

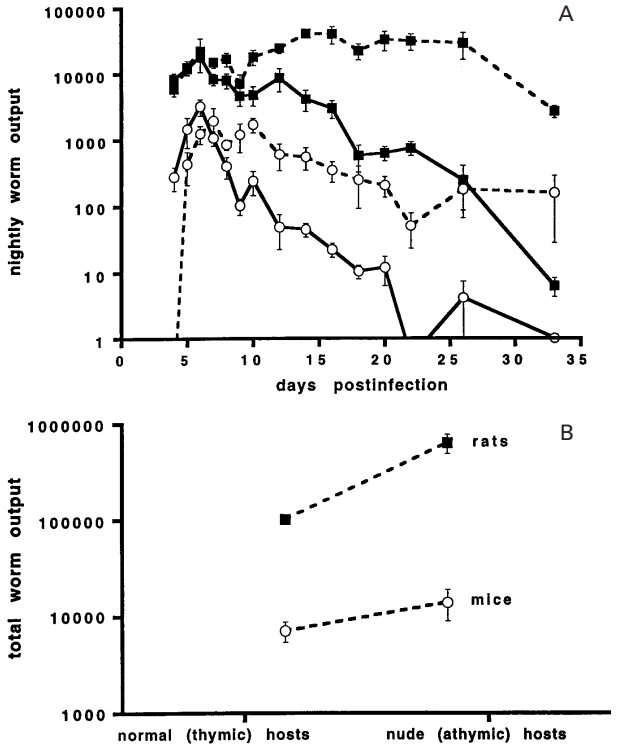

Fig. 5. Effect of host thymic status on reproductive success of *Strongyloides ratti* in rats (■: $n = 6$ nude; $n = 6$ normal) and mice (○: $n = 6$ nude; $n = 6$ normal). In (A), plotted values are nightly worm outputs: (——) normal animals; (– – –) nude animals. In (B), plotted values are total worm outputs. In both (A) and (B), error bars are ±1 S.E.M. In some cases, error bars are smaller than symbol.

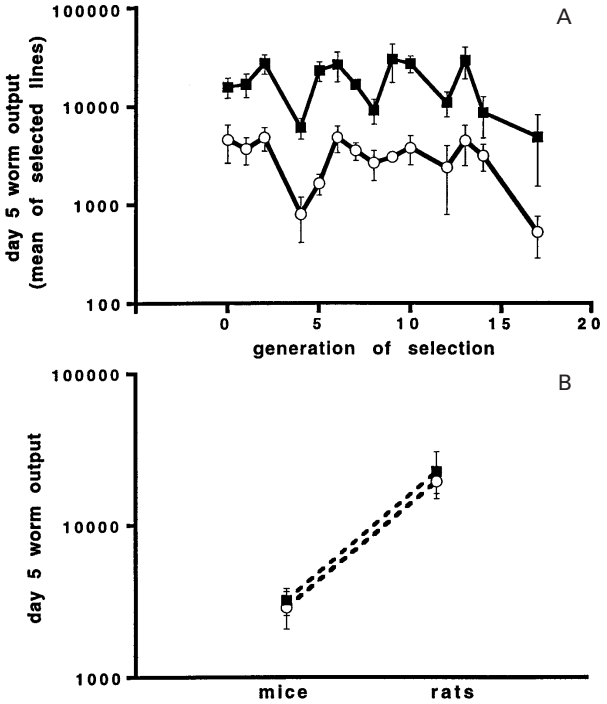

Fig. 6. Outcome of selection in rats and mice on day 5 p.i. worm output in *Strongyloides ratti*. In (A), plotted values are mean day 5 p.i. worm outputs of 'rat' lines (■: $n = 5$) and 'mouse' lines (○: $n = 5$) respectively. In (B), plotted values are mean day 5 p.i. worm outputs at generation 14 of 2 'rat' lines and 2 'mouse' lines each assayed in rats ($n = 3$ per line) and mice ($n = 3$ per line). Error bars are ±1 S.E.M. In some cases, error bars are smaller than symbol.

$P < 0{\cdot}05$; main effects: thymic status, $F_{1,20} = 24$, $P < 0{\cdot}0001$; host species, $F_{1,20} = 200$, $P < 0{\cdot}0001$). However, while total worm output from mice was not affected significantly by host thymic status, there was some evidence that once larval production reached its peak it declined less rapidly in nude mice than in normal mice. Using log–log regressions of nightly worm output on day post-infection to calculate a rate of decline (slope) for each individual host allowed these values to be used as independent data points in a one-factor ANOVA. This revealed that larval output declined about half as quickly in nude compared to normal mice ($F_{1,10} = 9{\cdot}85$, $P < 0{\cdot}05$). However, due to the relatively low worm outputs typical of the late stages of infection, this reduced decline had no appreciable impact on the total numbers of worms produced.

Outcome of selection

The trait under selection was worm output on day 5 p.i. Selection was continued for 18 generations. The mean day 5 p.i. worm outputs of selected lines between G0 and G17 are shown in Fig. 6A. At some generations (G3, G11, G15 and G16), day 5 output was not measured for logistical reasons. The difference in mean day 5 p.i. output between lines selected in rats and lines selected in mice did not change across generations (Spearman rank correlation: $r_s = -0{\cdot}13$, $P = 0{\cdot}65$).

Reciprocal cross-infection at G14 showed no effect of selection (Fig. 6B): worm output in both rats and mice was independent of the host species in which lines had been maintained prior to infection (day 5 p.i.: interaction of selection regime with host species: $F_{1,20} = 0{\cdot}39$, N.S.; main effects: selection regime, $F_{1,20} = 0{\cdot}03$, N.S.; host species, $F_{1,20} = 31$, $P < 0{\cdot}0001$). Thus, worm performance in mice and rats was unaffected by the host species which had harboured the previous 14 generations (Fig. 6B). Virtually identical results were obtained on days 8 and 11 p.i. (data not shown). Thus, there had been no measurable response by G14.

DISCUSSION

Even where the ecology of an organism is very habitat-restricted, this need not imply a proportionate degree of specialization. The problem is partly terminological (Futuyma & Moreno, 1988; Berenbaum, 1996). To some, the word 'specialization' implies the possession of habitat-specific adaptations. Undoubtedly, such adaptations are maintained in many parasitic taxa, but their existence is

usually inferred indirectly (Secord & Kareiva, 1996; Tompkins & Clayton, 1999). Phylogenetic study of host–parasite co-speciation has been the main focus of research into parasite specialization (Thompson, 1994; Hoberg, Brooks & Siegel-Causey, 1997; Paterson & Gray, 1997). The main assumption underpinning this approach is that parasites tend to speciate when their hosts speciate: where hosts go, parasites follow (Fahrenholz's Rule; e.g. Hafner & Nadler (1988); see Klassen (1992) for a history of this macroevolutionary tradition). Nonetheless, non-congruences of host–parasite phylogenies are ubiquitous and are often interpreted as reflecting 'host-switching' ('host-capture') events (Brooks, 1988). While host-specificity evolution can be profitably viewed at a macroevolutionary level, host-switching requires explanation in terms of micro-evolutionary processes.

The experiments reported here give an empirical account of some proximate factors shaping host-specificity in *S. ratti*. To our knowledge this is the first study to compare directly the performance of *S. ratti* in rats and mice. Worms had substantially higher reproductive success in rats compared with mice. This difference was due to lower establishment rates, earlier expulsion of established parasites and reduced per capita fecundity of *S. ratti* in mice. Reduced fecundity was at least as important as reduced establishment as a determinant of host specificity. The majority of these differences cannot be ascribed to the mouse T-dependent immune system, since worm output was significantly lower in athymic mice than in normal rats. These findings confirm that a more effective T-dependent response by mice to *S. ratti* infection (or less efficient evasion of a response by *S. ratti*) is not the major cause of reduced fitness of *S. ratti* in mice. Other candidate mechanisms for generating the difference in fitness of *S. ratti* in these two host species are other components of the rat and mouse immune systems (e.g. T-independent responses such as inflammatory and other non-specific responses), or non-immunological factors stemming from the different physiologies of rats and mice. It seems unlikely that the small size of mice compared to rats physically limits space and/or other resource availability. Previous studies have shown that output of *S. ratti* in C57/BL/6 mice increases linearly with inoculum size and reaches a plateau only when inocula sizes reach in excess of 3000 iL3s (Dawkins *et al*. 1980).

In the present study, 18 generations of experimental selection failed to modify the fitness of *S. ratti* in mice. Reciprocal assays of the fitness of selected lines in both host species confirmed that the original pattern of host-specificity displayed by this parasite remained intact. Artificial selection experiments sometimes fail to produce a response in the first few generations, the usual problem being small population size leading to genetic drift which retards a response (Falconer & Mackay, 1996). However, experience from the bulk of published artificial selection experiments is that if a response occurs at all it certainly does so within 18 generations (Falconer, 1989, 1992). Artificially imposed selection differentials may of course be larger than those imposed by natural selection and it may be the case that given enough time, *S. ratti* could be adapted to a new host species. Alternatively, the use of an established laboratory line derived from a single female may have limited genetic diversity in the base population. This is certainly possible, although this same isofemale line has responded rapidly to selection in the laboratory for other, apparently complex, life-history traits such as sexuality (Viney, 1996).

Serial passage is a standard tool of *in vivo* parasitology. Many studies describe attempts to adapt nematode parasites of mammals to new host species, but few involve the relevant controls, replication or reciprocal fitness assays required to test alternative evolutionary models of specialization (e.g. Bracket & Bliznick, 1949; Lindquist, 1950; Thatcher & Scott, 1962; Haley, 1966*a*; Lichtenfels, 1971; Forrester, 1971; Vincent *et al*. 1982; Lyons, Drudge & Tolliver, 1987). We are aware of only 3 studies using experimental natural selection followed by reciprocal fitness assays that also had adequate controls. All 3 were conducted with *Nippostrongylus brasiliensis*. Haley (1966*b*) selected *N. brasiliensis* (using a base population isolated from rats) for 40 generations in hamsters (*Mesocricetus auratus*). By the 8th generation, 'hamster' lines showed a significant increase in establishment in hamsters with an apparent selection limit being reached between the 16th and 24th generations. After 39 generations these lines were no less successful in rats than rat-selected control lines. Solomon & Haley (1966) selected lines of *N. brasiliensis* (again, isolated from rats) for success in mice. The response to selection was substantial and reached its limit after only 7 generations. A further 47 generations of selection failed to reduce the fitness of these lines in rats compared to control lines. In contrast, Westcott & Todd (1966) conducted a very similar experiment. They too reported a rapid increase in the performance of 'mouse' lines. However, this response was accompanied by a decrease in the fitness of 'mouse' lines in rats. Thus, what evidence there is regarding genetic correlations between fitness components on alternative hosts in *N. brasiliensis* is mixed – 1 study provides evidence of a trade-off, 2 do not. A salient feature of these experiments is the apparent ease with which a response to natural selection occurred, in contrast to the results reported here for *S. ratti*. *N. brasiliensis* is a cosmopolitan parasite of small rodents (Anderson, 1992) and it is possible that the base populations used in these experiments provided substantial genetic variation on which natural selection could act.

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