

The evolution of virulence

Andrew F. Read and Paul H. Harvey

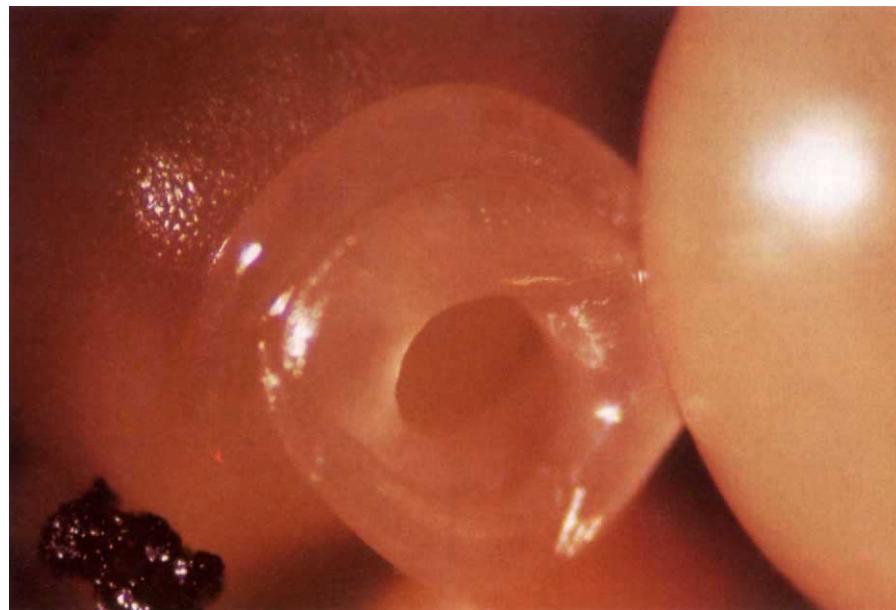
How virulent should we expect animal parasites to be? The answer depends, in part, on whether increased damage to the host improves the reproductive success of the parasite. Biologists have developed a theoretical framework within which the evolution of virulence can be analysed¹⁻⁴, and it has been demonstrated experimentally that virulence can evolve in response to alternative modes of parasite transmission⁵. Now, in an elegant comparative study published in *Science*⁶, Allen Herre shows how differences in the likely mode of transmission correspond with expected differences in virulence in natural populations.

For parasites whose offspring infect the offspring of their host (vertical transmission), any behaviour by the parasite that decreases the fecundity of its host (and thereby that of the parasite itself) is unlikely to be favoured by natural selection. In contrast, parasites whose offspring are not dependent on those of their host (horizontal transmission) are expected to become more virulent if that results in the production of an increased number of parasite young.

In a test of this idea, Bull *et al.*⁵ propagated populations of phage-infected *Escherichia coli* in two ways. In one, phage replication was wholly dependent on host reproduction. In the other, phage could be transmitted vertically and horizontally. The two selection regimes had the expected effects on host fitness: infected bacteria in the vertically transmitted lines increased in density much more quickly than those in the lines where horizontal transmission could occur. Genetic changes in both host and parasite were responsible for the evolved differences in virulence.

The generality of conclusions from well controlled experiments can often be tested by comparative studies⁷. For example, Ewald has argued that variation in virulence among a variety of human diseases may be accounted for by differences in the relationship between virulence and transmission⁸. In his view, directly transmitted diseases such as common colds generally have lower virulence than vector-borne diseases such as malaria because transmission rates in the former are higher if infective hosts continue to come into contact with other individuals. In contrast, host immobility is beneficial to vector-borne diseases because vector-avoidance behaviour is minimized. Ewald's surveys of human diseases⁸ generally fit this pattern. But such broad surveys necessarily include a wide range of parasites, which differ not only in transmission routes but in many

other aspects of their natural history. As one of us wrote only two years ago, "comparisons of the virulence of parasite taxa utilizing different transmission routes from similar hosts are not yet possible"⁹. Herre's study⁶ shows that they now are.



A twist in the tail — *Parasitodiplogaster obtunema*, one of the direct life-cycle nematodes, parasitic on fig wasps, central to the work described here. (Photo, Allen Herre.)

Herre examined a group of direct life-cycle nematodes (*Parasitodiplogaster* spp.) each specific to one of eleven Panamanian fig wasp species (*Pegoscapus* spp., *Tetrapus* sp.). Because of the peculiar natural history of these hosts, the relative importance of horizontal and vertical transmission differs among parasite species.

Gravid female fig wasps enter figs, lay eggs and die. Their progeny mate inside the fig before the young females disperse to new figs. The nematode generations are intimately connected with those of their hosts. For part of their life cycle, nematodes consume the body of the adult female fig wasp. After the death of an infected foundress in a fig, about six or seven nematode adults emerge from the carcass, mate and lay eggs in the same fig. The eggs hatch synchronously with the emergence of the wasp larvae, and the nematode larvae infect young female fig wasps before they disperse. Because the wasps lay all their eggs in a single fig, Herre estimates nematode virulence as the relative lifetime reproductive success of infected compared with uninfected wasps, when each lays on its own in a fig.

A consequence of fig-wasp life-cycles is that the number of female wasps

laying in a fig determines the opportunity for horizontal transmission by the nematodes. If only one female is present, a nematode's offspring must infect the offspring of that host. So selection should favour benign parasites that limit the destruction of their hosts. But where there are more foundresses per fig, parasite reproductive success depends less on the fecundity of its host because other wasps are laying potential hosts. It seems reasonable to assume that greater

consumption of host resources by nematodes causes reductions in host fecundity, and that, as in other parasitic nematodes¹⁰, bigger worms produce more eggs. As a consequence, greater virulence should be favoured if enough offspring of other wasps can be infected to more than compensate for the subsequent loss of extra offspring from the current host.

Herre shows that this is indeed the

1. Levin, S. & Pimentel, D. *Am. Nat.* **117**, 308–315 (1981).
2. Anderson, R. M. & May, R. M. *Parasitology* **85**, 411–426 (1982).
3. May, R. M. & Anderson, R. M. *Proc. R. Soc.* **B219**, 281–313 (1983).
4. Bremermann, H. J. & Pickering, J. J. *theor. Biol.* **100**, 411–426 (1983).
5. Bull, J. J., Molineux, I. J. & Rice, W. R. *Evolution* **45**, 875–882 (1991).
6. Herre, E. A. *Science* **259**, 1442–1445 (1993).
7. Harvey, P. H. & Pagel, M. D. *The Comparative Method in Evolutionary Biology* (Oxford University Press, 1991).
8. Ewald, P. W. *A. Rev. Ecol. Syst.* **14**, 465–485 (1983).
9. Read, A. F. & Schrag, S. J. *Parasitology Today* **7**, 296–297 (1991).
10. Skorping, A., Read, A. F. & Keymer, A. E. *Oikos* **60**, 365–371 (1991).
11. Dye, C. & Davies, C. R. *Trends Ecol. Evol.* **5**, 237–238 (1990).
12. Frank, S. A. *Proc. R. Soc.* **B250**, 195–197 (1992).
13. Charnov, E. L. *The Theory of Sex Allocation* (Princeton University Press, 1982).
14. Frank, S. A. *Florida Ent.* **66**, 42–75 (1983).
15. Hamilton, W. D. *Science* **156**, 477–488 (1967).
16. Hamilton, W. D. in *Sexual Selection and Reproductive Competition in Insects* (eds Blum, M. S. & Blum, N. A.) 167–220 (Academic, New York, 1979).
17. Herre, E. A. *Nature* **329**, 627–629 (1987).

case. In those species where almost all broods are initiated by one foundress, he found that parasitism had no detectable effect on fitness. But in species where less than a third of broods are founded by a single wasp, parasites reduced the reproductive success of their hosts by up to 16 per cent. The relationship between virulence and the frequency of single-foundress broods was roughly linear. Thus, the wasp–nematode relationships ranged from commensal to clearly parasitic, in accord with their different transmission routes.

Comparisons of virulence of closely related parasites in hosts with which they have co-evolved automatically control for many third variables which potentially confound such analyses. Comparisons of the same host–parasite system when transmission is likely to vary, either between populations or over time, may also prove profitable. For example, Dye and Davies¹¹ have suggested that fluctuations in the virulence of gerbil leishmaniasis (an animal model of the human

disease) are a consequence of seasonal variation in transmission dynamics.

Now that observations are beginning to support theories about the relationship between virulence and transmissibility in the evolution of pathogenicity, the way is open for further theoretical developments. Many of the same theoretical issues arise in the study of the evolution of sex ratio in group-structured populations^{1,4,12}, a topic which has spawned some of the most impressive fits between quantitative predictions of evolutionary theory and field data^{13,14}. It is no accident that the curious natural history of fig wasps played an important part in that work as well^{15–17}. □

Andrew F. Read is in the Institute of Cell, Animal and Population Biology, University of Edinburgh, West Mains Road, Edinburgh EH9 3JT, UK. Paul H. Harvey is in the AFRC Unit of Behaviour and Ecology, Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3PS, UK.

heidelbergensis) should be recognized to fill any taxonomic void between *H. erectus* and Neanderthals, and the extent to which internal, rather than between-taxon, variation is responsible for differences between the specimens^{4–7}. On this last point, I have argued that differences between large specimens (such as the Petralona cranium) and small specimens (such as the Steinheim cranium) do warrant a degree of taxonomic separation⁵, whereas others consider that the differences are due more to internal population variation such as sexual dimorphism⁴.

The Atapuerca skeletal sample is large by the standards of any other Middle Pleistocene hominid site, so it provides an unprecedented opportunity to examine the internal morphological and metrical variation of what is assumed to represent a penecontemporaneous sample of individuals of different ages and sex. This is important for questions of taxonomy, because we can observe the relative frequency of *H. erectus* and Neanderthal characters in the sample, and for phylogeny, because questions of character polarity may be resolved (for some parts of the skeleton there were no Middle Pleistocene data before the discovery of the bones at Atapuerca).

The new paper¹ and Table 2 list the extent to which the Atapuerca sample shows some of the characters typical of *H. erectus* (late European), Neanderthals, and modern *H. sapiens*. The absence of most of the distinctive *H. erectus* features in the Atapuerca sample is evi-

PALAEOANTHROPOLOGY

Secrets of the Pit of the Bones

Chris Stringer

SOME 300,000 years ago, the remains of at least 24 people somehow found their way into the Sima de los Huesos, a small chamber deep within a cave in the Sierra de Atapuerca, northern Spain. There they became fossilized. Although the mechanism of accumulation of the jumbled bones presents a puzzle, the discoveries of the latest in a long series of excavations by Spanish workers, reported on page 534 of this issue¹, seem not only to have settled the question of the affinities of the Atapuerca hominids, but also promise to clarify our understanding of the evolution of humans in Europe.

Debate about the European fossil hominid record has concentrated on the Late Pleistocene interface between Neanderthals and early modern humans in the period between about 40,000 and 30,000 years ago (40–30 kyr)^{2,3}. This emphasis has tended to eclipse developments in analysis of the Middle Pleistocene record, which begins with the Mauer (Heidelberg) mandible (estimated age about 500 kyr) and ends at about 130 kyr, after which time undoubted Neanderthals were present in Europe. A possible chronological sequence for some of the more important hominid finds is shown in Table 1, together with proposals as to their taxonomy.

There are two main issues in the study of the Middle Pleistocene sequence. Can

the species *Homo erectus* be recognized in the European fossil record? And how far back can the Neanderthal lineage be traced? Other questions that follow are whether other species (for instance *H.*

TABLE 1. Four interpretations of the European hominid sequence

Age (kyr)	Fossil hominids	a	b	c	d
30	Early modern	<i>H. sapiens sapiens</i>	Modern <i>H. sapiens</i>	<i>H. sapiens</i>	<i>H. sapiens</i>
50	Late Neanderthals	<i>H. sapiens neanderthalensis</i>			
120	Saccopastore				
	Biache			<i>H. neanderthalensis</i>	
220	Ehringsdorf Pontnewydd Reilingen? Swanscombe? Steinheim?	<i>H. sapiens steinheimensis</i>	Archaic <i>H. sapiens</i>		<i>H. neanderthalensis</i>
300	Atapuerca Petralona? Bilzingsleben Vértesszöllös? Arago?			<i>H. heidelbergensis</i>	
500	Mauer?	<i>H. erectus</i>			

Scheme a recognizes two species (*sapiens*, represented by three subspecies, and *erectus*), b only one (*sapiens*, in 'modern' and 'archaic' forms), c three (*sapiens*, *neanderthalensis* and *heidelbergensis*) and d two (*sapiens*, *neanderthalensis*). Assuming that the Mauer mandible belongs taxonomically with the subsequent sample, the new Atapuerca evidence appears to favour scheme b, or d (my own preference).