

Table 2. Ranking of categories according to the proportion of species associated with emerging diseases.

(Species in the database fell into 26 categories, seven of which were excluded as they contained less than ten species.)

transmission route	zoonotic status	taxonomic division	total number of species	number of emerging species	proportion of species emerging
indirect contact	zoonotic	viruses	37	17	0.459
indirect contact	zoonotic	protozoa	14	6	0.429
direct contact	zoonotic	viruses	63	26	0.413
direct contact	non-zoonotic	protozoa	15	6	0.400
indirect contact	non-zoonotic	viruses	13	4	0.308
direct contact	non-zoonotic	viruses	47	14	0.298
vector borne	zoonotic	viruses	99	29	0.293
vector borne	zoonotic	bacteria	40	9	0.225
indirect contact	zoonotic	bacteria	143	31	0.217
vector borne	zoonotic	protozoa	26	5	0.192
direct contact	zoonotic	bacteria	130	20	0.154
indirect contact	zoonotic	fungi	85	11	0.129
direct contact	zoonotic	fungi	105	13	0.124
vector borne	zoonotic	helminths	23	2	0.087
direct contact	non-zoonotic	bacteria	125	7	0.056
indirect contact	non-zoonotic	bacteria	63	3	0.048
indirect contact	non-zoonotic	fungi	120	3	0.025
direct contact	non-zoonotic	fungi	123	3	0.024
indirect contact	zoonotic	helminths	250	6	0.024

indirect contact, 28% by vectors, and for 6% the transmission route is not known.

Risk factors for emergence were first analysed separately and the relative risks are presented in table 1a. One hundred and thirty-two emerging pathogen species (75%) are zoonotic (electronic Appendix A). This is substantially more than expected if zoonotic and non-zoonotic species were equally likely to emerge, and corresponds to a relative risk of 1.93. This result is retained when the analyses are repeated at the genus rather than the species level; 78 out of 96 emerging genera are zoonotic (81%), compared with 235 out of 376 non-emerging genera (62%). This corresponds to a relative risk of 2.20, similar to that for species, suggesting that the result is robust. However, different risks of emergence are also associated with different taxonomic divisions; viruses and protozoa are overrepresented and fungi and helminths are underrepresented among emerging species (electronic Appendix A). A higher risk of emergence is also associated with vector-borne transmission. These analyses suggest that zoonotic pathogens are more likely to emerge than non-zoonotic pathogens, but that the strength of the effect may be affected by pathogen taxonomy and transmission routes.

Pathogen taxonomy, zoonotic status, and transmission routes are not independent (figure 1). For example, virtually all helminths are zoonotic and transmitted by indirect contact and there are very few vector-borne fungi. To investigate how these different risk factors combine to affect the likelihood of pathogen emergence, two approaches were taken. First, the effect of zoonotic status within individual taxonomic and transmission route categories was investigated (table 1b). The effect of zoonotic status varies markedly among the taxonomic groups. Zoonotic bacteria and fungi were more than three times as likely to emerge than non-zoonotic

bacteria and fungi (relative risks of 3.79 and 7.14, respectively). However, the opposite was true for helminths with zoonotic species far less likely to emerge than non-zoonotic ones (relative risk of 0.19). For viruses and protozoa, zoonotic status appears to make little difference to the risk of emergence (relative risks of 0.96 and 0.74, respectively). Zoonotic pathogens show a higher probability of emerging if they are transmitted by direct or indirect contact (relative risks of 2.13 and 2.60, respectively), but among vector-borne pathogens zoonotic status made virtually no difference (relative risk of 0.97). Second, all species were divided into categories based on taxonomic division, transmission route and zoonotic status (table 2). Categories with less than ten species were excluded and the rest ranked by the percentage of species emerging. The most striking result is that viruses and protozoa account for all of the top seven categories, all with more than 29% of the species emerging. The next strongest pattern was that zoonotic pathogens tended to rank above non-zoonotic pathogens, although zoonotic helminths transmitted by indirect contact showed a very low proportion of emerging pathogens (2%). No obvious pattern was seen associated with route of transmission.

#### 4. DISCUSSION

The majority of pathogen species causing disease in humans are zoonotic (868 species, i.e. 61% of the total; electronic Appendix A). In agreement with the original hypothesis, zoonotic species are overall twice as likely to be associated with emerging diseases than non-zoonotic species. However, more detailed analysis shows that there are also very strong effects of taxonomy on the probability that a pathogen will be classed as emerging. Viruses and protozoa are especially likely to emerge and helminths

very unlikely to emerge irrespective of their transmission routes or zoonotic status. Our attempt to identify risk factors for emergence points strongly towards taxonomic and zoonotic status effects.

Interpretation of these results is complicated by uneven distributions of organisms across the taxonomic divisions, transmission routes and zoonotic status, and non-independence between these variables. Helminths are especially likely to be associated with zoonoses: 95% of helminth species pathogenic to humans are known to be zoonotic, compared with 76% of viruses and prions, 65% of protozoa, 50% of bacteria and rickettsia, and just 38% of fungi. In addition, zoonoses are relatively likely to be transmitted indirectly (including transmission by intermediate hosts) or by vectors, suggesting that these transmission routes may be associated with lower host specificity (Woolhouse *et al.* 2001). These two observations are not independent; for example, almost all helminths are transmitted by these routes. The observation that the route of transmission of over 200 human pathogens (both zoonotic and non-zoonotic) remains unknown emphasizes the need for improved understanding of the biology of infectious agents in general.

An additional factor that may be involved in emergence is transmissibility between humans, because the incidence of new infections can also be highly sensitive to small changes in transmission rates within a local human population. Rigorous analysis is precluded by the absence of data: for 620 species of infectious agents (44%) the cited references contain no information on whether they are transmissible between humans. However, for species where information is available, the pattern is highly suggestive. Human-to-human transmissibility is a risk factor for emergence across all pathogens, with a relative risk of 2.60.

The most important finding reported here is that emerging pathogens are not a random selection of all human pathogens. The next challenge is to explain why some kinds of pathogen—such as zoonotic viruses and protozoa transmitted by indirect contact (table 2)—are likely to emerge while others are not. It must be emphasized that disease emergence is to some extent subjectively defined and so any analysis is prone to biases in reporting, recognition and the availability of information, as may be associated with different taxa or different geographical regions. Indeed it is sometimes suggested that emerging disease trends at least partly reflect biases among the research community. Nonetheless, we anticipate that pathogen biology also contributes to the likelihood of emergence, including such factors as genetic diversity, generation time and existence of a reservoir (whether zoonotic or environmental).

This study considers the diversity of pathogens causing disease in humans, and not the public health burden imposed by these diseases. Although mortality and morbidity estimates are now available for some common infectious diseases (Murray *et al.* 1994; Murray & Lopez 1996), such data cannot always be attributed to individual species of pathogen and the health burden for the vast majority of human pathogens remains completely unquantified. Moreover, the importance of zoonoses is often to be found in the origins rather than the severity of disease outbreaks. While direct trans-

mission from animals is important for some zoonotic pathogens, such as rabies, *Brucella melitensis* and *Mycobacterium bovis*, for others, such as influenza A and Dengue, transmission from animals is important mainly in the origin of outbreaks; the majority of humans are infected by other humans. This argument is well illustrated by the HIVs: these viruses emerged into humans from a primate reservoir, but rapidly evolved and are no longer regarded as zoonotic. Nonetheless, animal and human diseases can be closely associated; recent examples include Rift Valley fever in Kenya and Somalia (WHO Press Release 1998), Nipah virus in Malaysia and Singapore (Chua *et al.* 2000), West Nile virus in the United States (Lanciotti *et al.* 1999) and Hendra virus in Australia (Westbury 2000). The management of these pathogens poses challenges outside the scope of traditional medical practice and demands a much closer collaboration between medical and veterinary researchers than has tended to occur in the past.

In conclusion, this study is, as far as we are aware, the first to identify risk factors for human disease emergence. This type of analysis, which, hopefully, will be refined and improved in the future, is essential if emerging diseases are not always to be regarded as a set of individual case studies with no underlying general principles.

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