

Heterogeneities in schistosome transmission dynamics and control

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SUMMARY

We review the theoretical framework for exploring the impact of individual and spatial heterogeneities in patterns of exposure and contamination and on the basic reproduction number, R_0 , for human schistosomes. Analysis of water contact data for 5 communities in Zimbabwe and Mali suggests that the impact is substantial, increasing R_0 by factors of up to 6.5, mostly due to highly overdispersed distributions of contact rates among individuals. Several practical conclusions emerge: concentration of contacts at a single site should be avoided; the impact of control targeted at certain sites cannot be predicted without knowledge of how individuals' contacts are distributed among sites; control programmes targeted at individuals or sites contributing most to transmission can be very efficient but, conversely, will be ineffective if any of these individuals or sites are missed.

Key words: basic reproduction number, exposure, heterogeneity, schistosomiasis, water contact.

INTRODUCTION

Transmission of schistosomes requires contact between the definitive host and water containing the intermediate host snails. Such contact is related both to exposure and contamination, transmission to and from the definitive host respectively. The rate of exposure depends on the rate of water contact, weighted by a number of factors including the activity undertaken (including the use of soap), the area of skin exposed, the time of day (since cercarial emergence has a marked diurnal rhythm) and the duration of exposure (Chandiwana & Woolhouse, 1991; Etard & Borel, 1992). The rate of contamination also depends on the rate of water contact, weighted by the degree to which the activity undertaken is associated with urination or defecation or, for example, contamination with excreta while washing or washing clothes.

The pattern of exposure and contamination can exhibit a number of heterogeneities, illustrated diagrammatically in Fig. 1. Individuals may differ in their exposure/contamination rates; water contact sites may differ in the net rates of exposure/contamination occurring at the site; and individuals may differ in the way in which they distribute their exposure/contamination among different sites – this

is referred to as the individual's contact pattern. There are many other ways in which transmission may be heterogeneous: individuals may differ in their innate or acquired resistance to infection and their potential to excrete schistosome eggs, perhaps due to age, sex, or genetic or nutritional factors; water contact sites may differ in their hydrology, chemistry or physical environment, influencing the ability of miracidia and cercariae to locate and infect their target hosts, or in the susceptibility of the snail population at the site, perhaps due to genetic factors. For the purposes of this paper, however, we will focus on heterogeneities in patterns of exposure and contamination.

Several studies have shown that heterogeneities in transmission rates affect the basic reproduction number, R_0 . For schistosomes, R_0 is defined as the average number of mated female schistosomes produced by 1 mated female schistosome during her life-time in the absence of any density-dependent constraints on population growth. Clearly, if R_0 is greater than 1 then schistosome infection can spread through the host population, resulting in epidemic or endemic infection. However, if R_0 is less than 1 then infection will tend to die out as each female cannot replace herself in the host population. Because R_0 is a measure of *potential* transmission it is related to the total numbers of humans and snails rather than the numbers that are actually infected.

In general, heterogeneities in the transmission of infectious agents act to increase R_0 (Anderson &

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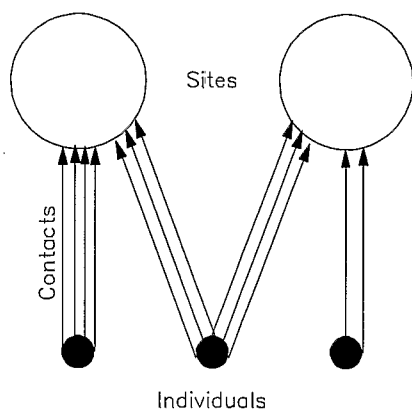


Fig. 1. Diagrammatic representation of heterogeneities in water contact rates. Each arrow represents 1 water contact by 1 individual/unit time. Three types of heterogeneity are illustrated: (1) different net contact rates by the 3 individuals; (2) different net contact rates at the 2 sites; (3) differences in the way individuals distribute their contacts among sites, the contact pattern.

May, 1991; Woolhouse *et al.* 1997) simply because transmission is efficiently focused within a core fraction of high transmitters. This applies whether the heterogeneities result from spatial substructuring of the host population for directly transmitted viral infections (Anderson & May, 1991), differences in rates of change of sexual partners for sexually transmitted diseases (Anderson & May, 1991), differences in vector biting rates for arthropod-borne infections (Dye & Hasibeder, 1986) or, as here, water contact rates for water-borne infections (Barbour, 1978; Woolhouse, Watts & Chandiwana, 1991). An important consequence concerns the design of disease control programmes. In general, eradication by non-targeted control measures (for schistosomes these might be mass chemotherapy or blanket mollusciciding) is made more difficult by heterogeneities in transmission because these tend to increase R_0 . However, targeted control measures (for schistosomes these might be targeted chemotherapy or focal mollusciciding) may be relatively efficient, provided that control can be directed at individuals or sites contributing most to transmission. For a variety of infections R_0 can be reduced by at least 80% by targeting 20% of the population (Woolhouse *et al.* 1997); this result is referred to as the 20/80 rule.

In this paper we review the theoretical framework for analysing the impact of heterogeneous transmission on R_0 for human schistosome infections, including the effects of spatial heterogeneities in intermediate host snail densities, apply this framework to 5 data sets reporting water contact patterns in communities in Zimbabwe and Mali, and consider the implications for the design of schistosomiasis control programmes, especially those involving focal molluscicide application.

METHODS

Mathematical model

The mathematical model follows Barbour (1978), Dietz (1979), Anderson & May (1991) and Woolhouse *et al.* (1991). We consider schistosomes infecting a constant human population of P individuals who make water contact at L sites. Here, a site is considered a spatially discrete water body or part of a water body containing a well-mixed population of N snails. The model describes the rates of change in the number of schistosomes in each individual i , M_i (where $i = 1$ to P), and in the fraction of infected snails at each site, y_j (where $j = 1$ to L). The rate of exposure by individual i at site j is denoted η_{ij} and the rate of contamination of the water with excreta by individual i at site j is denoted κ_{ij} .

The dynamics of schistosome transmission in this system are represented by the set of coupled differential equations:

$$\frac{dM_i}{dt} = \alpha(\sum_j \eta_{ij} N y_j) - \gamma M_i, \quad (1)$$

$$\frac{dy_j}{dt} = \beta(\sum_i \kappa_{ij} M_i)(1 - y_j) - \mu y_j, \quad (2)$$

where α is the number of schistosomes acquired/unit exposure/infected snail; β is the probability of infection/snail/schistosome/unit contamination; γ is the *per capita* mortality rate for schistosomes; μ is the *per capita* mortality rate of infected snails. This model ignores complications such as pre-patent infections of snails, schistosome mating, age-dependent parameter values and acquired immunity. These aspects are considered elsewhere (Woolhouse, 1991, 1996) but are not essential to the arguments to be developed in this paper.

For this model the basic reproduction number, R_0 , is proportional to ϵ , the dominant eigenvalue of the L by L matrix with elements $u_{jk} = \sum_i (\eta_{ij} \kappa_{ik})$ where $k = 1$ to L . This general result is useful but rather abstract so it is helpful to consider a number of special cases and developments of the result in order better to understand its implications.

Individual heterogeneity

If $L = 1$ then we have only to consider heterogeneity in individuals' exposure rates and contamination rates. In the absence of individual heterogeneity then R_0 is simply proportional to the product of the mean rates of exposure and contamination and this proportionality is implicit in all the following equations. If there is individual heterogeneity then furthermore

$$R_0 \propto 1 + CV(\eta_i) CV(\kappa_i) r_{\eta\kappa}, \quad (3)$$

where CV represents the coefficient of variation and $r_{\eta\kappa}$ is the correlation between individual rates of

exposure and contamination. Thus R_0 is higher if the variances of rates of exposure and contamination are high, i.e. there is a high degree of heterogeneity between individuals, provided that exposure and contamination rates are positively correlated. If they are not correlated then heterogeneity between individuals has no impact and if they are negatively correlated heterogeneity acts to reduce R_0 , although the latter seems unlikely in practice. Clearly, if an individual's exposure and contamination rates are both proportional to their rate of water contact then $r_{\eta\kappa} = 1$ and we obtain

$$R_0 \propto 1 + CV^2(\lambda_i), \quad (4)$$

where λ_i represents the total rate of exposure of individual i across all sites and CV^2 is equivalent to the standardized variance (i.e. variance over mean squared). This illustrates the general conclusion that heterogeneities in transmission rates increase R_0 .

Site heterogeneity

If $L > 1$, there is no heterogeneity between individuals, and each individual's contacts are equally distributed among L sites then R_0 is proportional to $1/L$. More generally, if there is heterogeneity between sites Equation (3) again applies but means, standard deviations and correlations refer to sites rather than individuals. In this case, it is easier to imagine a negative correlation between exposure and contamination, for example, if some water contact sites are used for sanitation and others are used for different purposes. This would, of course, decrease R_0 . Alternatively, if both net exposure and contamination rates at a site are proportional to the rate of water contact then we obtain

$$R_0 \propto 1 + CV^2(\lambda_j), \quad (5)$$

where λ_j represents the total rate of contact at site j by all individuals.

Heterogeneity in contact pattern

In general, there are many ways in which individuals may distribute their water contacts among different sites, and hence many possible values for ϵ even for the same set of λ_i and λ_j values. There is one instructive special case, however, where all individuals make the same proportion of their contacts at each site. In this case

$$R_0 \propto (1 + CV^2(\lambda_i))(1 + CV^2(\lambda_j)), \quad (6)$$

Again, heterogeneity in contact rates between individuals and between sites both increase R_0 (given that exposure and contamination rates are positively correlated both across individuals and across sites). In general, the impact of contact pattern is greater than indicated by Equation (6) if each individual tends to concentrate its contacts at one site, referred to as selective use. Conversely, the impact is less than

indicated by Equation (6) if each individual tends to spread its contacts evenly over all sites, referred to as even use.

Spatial heterogeneity in snail density

So far we have assumed that all sites support the same number of density of snails. If snail densities vary between sites then we replace N in Equation (1) by N_j and, ignoring heterogeneity in individual water contact rates, we obtain

$$R_0 \propto 1 + CV^2(\lambda_i) + 2CV(\lambda_j) CV(N_j)r_{\lambda N}. \quad (7)$$

Thus, spatial heterogeneity in snail density only has an impact on R_0 if snail densities are correlated with contact rates across sites; if this correlation is negative then the effect is to reduce R_0 .

Field data

Data on human water contact behaviour and snail densities are available from studies of 2 communities in Zimbabwe (Chandiwana & Woolhouse, 1991; Woolhouse *et al.* 1997), and 3 communities in Mali (Etard, Audibert & Dabo, 1995). The Zimbabwe data were obtained from Nyamakari and Nahoon farms in the Burma Valley region. At Nyamakari all water contacts made by all individuals at all contact sites during daylight hours were recorded every day over a 14-day period; at Nahoon the same procedure was carried out on each of 42 days over a 2-month period. The Mali data were obtained from the villages of Maniale, Medina Coura and Dogofry Ba in the Segou region. In this study all water contacts made by individuals comprising a designated study population on 1 day at a single site were recorded, and observations were rotated among sites over a 7-month period. Details of the size of the studies are given in Table 1. In all of these studies water contact sites were clearly discrete (although we recognize that this is not the case in all field situations) and observations were made during the schistosome transmission season. In each case a contact was defined as a single visit to a site during which part or all of the skin was exposed to the water. This definition is simplistic in that contacts vary in the degree of potential exposure to infection and in the likelihood of contamination of the water with excreta, but captures the essential features well enough for current purposes (see Chandiwana, Woolhouse & Bradley, 1991), with the proviso that no direct estimates of the correlation between exposure and contamination rates across individuals or across sites are possible.

For each study an estimate of relative snail densities at each of the contact sites was made on at least 1 occasion by scooping. Here, we consider only densities of the snail intermediate hosts for *S. haematobium*, *Bulinus globosus* in Zimbabwe and *B. truncatus* in Mali.

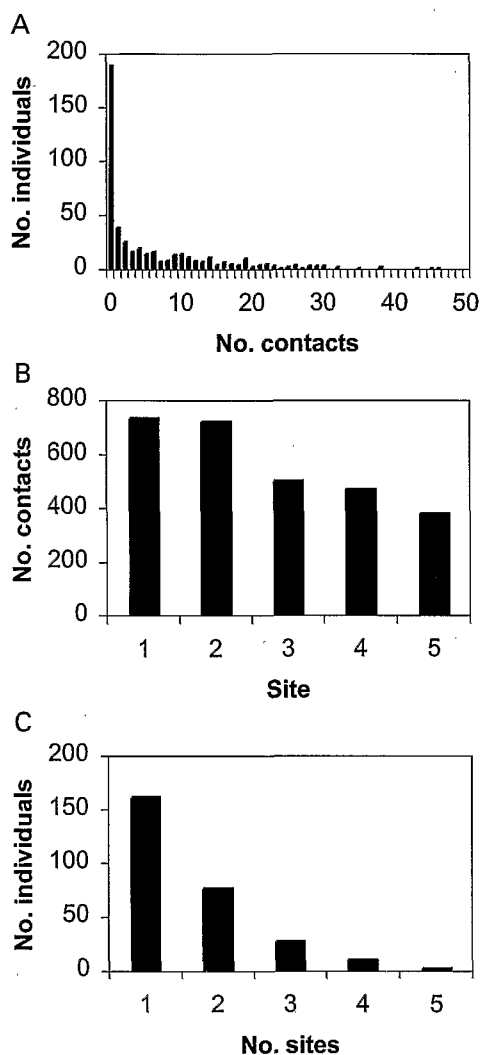


Fig. 2. Field data from Nyamakari, Zimbabwe. (A) Frequency distribution for the number of contacts made over the entire observation period by each individual in the study population. (B) Total number of contacts made over the entire observation period at each of the water contact sites monitored, ranked in descending order. (C) Frequency distribution for the number of sites used over the entire observation period by all individuals in the study population that made at least 1 contact.

RESULTS

Overall, the field data provide estimates of P , L , λ_{ij} , N_j and $r_{\lambda N}$. For current purposes we shall assume that exposure and contamination rates are perfectly correlated across individuals and across sites; the analysis should therefore be regarded as providing upper bounds for effects on R_0 . Here, we do not make estimates of absolute values of R_0 and are concerned only with relative values.

A consistent and striking feature of the data is the highly overdispersed distribution of individual water contacts (Figs 2A–6A). The mean contact rates varied from 0.14/individual/day in Nahoon to

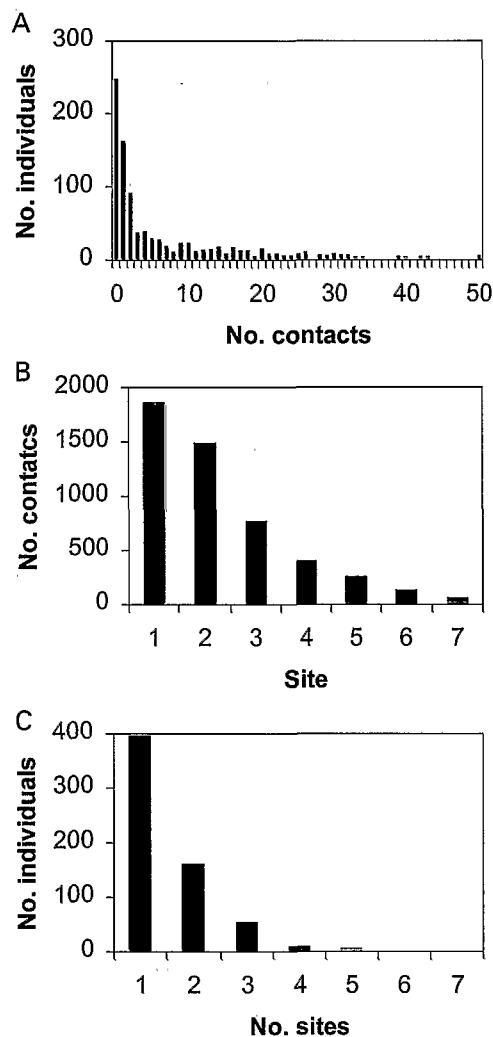


Fig. 3. Field data from Nahoon, Zimbabwe. As legend for Fig. 2.

1.55 in Dogofry Ba but the variances were consistently much higher than the means. Most individuals made few or no contacts and few individuals made very many contacts i.e. the majority of the contacts were made by a small minority of the population. Substituting coefficients of variation in individual contact rates into Equation (4) gives estimates of the increase in R_0 in the range 2.4 to 3.8 (Table 1).

The distributions of contacts among sites also tended to be overdispersed, although this was not as marked as for individuals' contacts (Figs 2B–6B). The mean contact rates varied from 16.4/site/day in Nahoon to 65.5 in Dogofry Ba. Substituting coefficients of variation in site contact rates into Equation (5) gives estimates of the increase in R_0 in the range 7% to 90% (Table 1).

An indication of contact patterns is obtained by showing the numbers of individuals recorded at 1 to L different sites (Figs 2C–6C). This shows that most individuals tend to use just one or two of the available sites, corresponding to selective use as

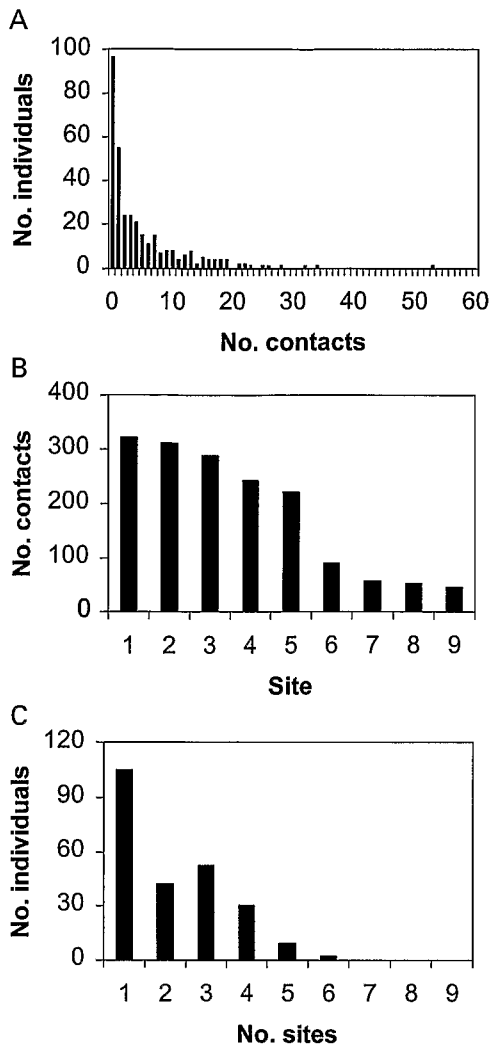


Fig. 4. Field data from Maniale, Mali. As legend for Fig. 2.

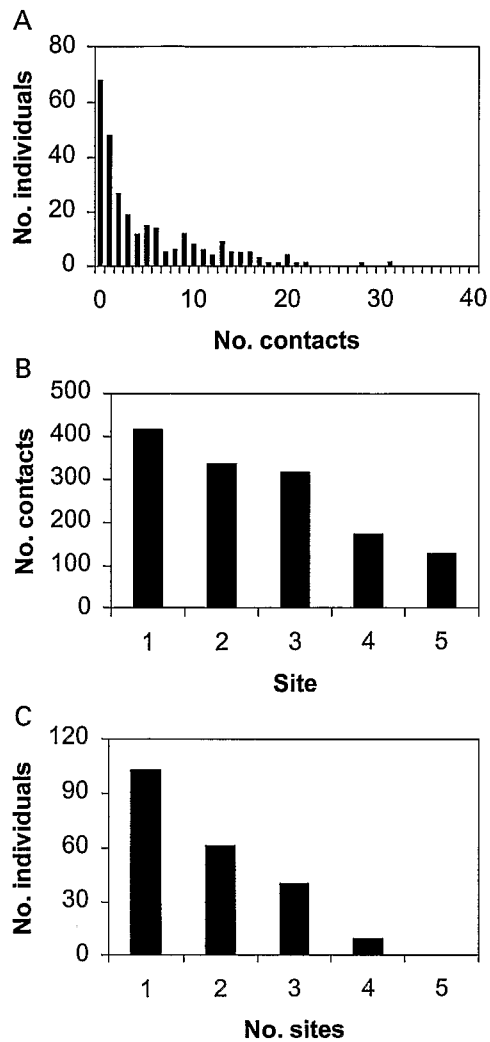


Fig. 5. Field data from Medina Coura, Mali. As legend for Fig. 2.

defined above. This pattern largely arises because adult males and adult females tended to use different sites, but with less discrimination shown by children. The effects of contact pattern can be quantified by calculating ϵ , which gives the overall impact of heterogeneities in λ_{ij} values and dividing by the contribution of individual and site variance without regard to contact pattern, as given by Equation (6). Because there is a tendency towards selective use the impact of contact pattern is to increase R_0 by between 2% and 37% (Table 1). The overall impacts of heterogeneities in contact rates are therefore substantial, giving estimated increases in R_0 in the range 3.4 to 6.5 (Table 1).

In no case was there a statistically significant correlation across sites between number of contacts and relative snail density. This is perhaps not surprising given the small numbers of sites involved and therefore the low statistical power. The correlation coefficients observed ranged from -0.64 to $+0.43$ (Table 1). Substituting into Equation (7) these values would give a change in R_0 of -66% to

$+34\%$ respectively over the effects due to heterogeneity in site contact rates alone.

These results have a number of implications for schistosomiasis control programmes. For all 5 populations considered here, R_0 can be reduced by more than 80% by preventing transmission in just 20% of the population, that is, these data conform to the 20/80 rule. The impact of targeting individuals can be further enhanced by consideration of their contact patterns. For a given contact rate, individuals making selective use of the most heavily used contact sites contribute most to R_0 . However, this enhanced impact is difficult to quantify in the absence of an efficient algorithm for ordering individuals by their estimated contributions to R_0 , where these estimates incorporate heterogeneities in contact pattern.

The impact of targeting control (e.g. regular mollusciciding) at the sites with the highest contact rates is shown, for the field studies analysed here, in Fig. 7. The results suggest that substantial reductions in R_0 can be achieved with control at only some sites but, conversely, that there may be relatively

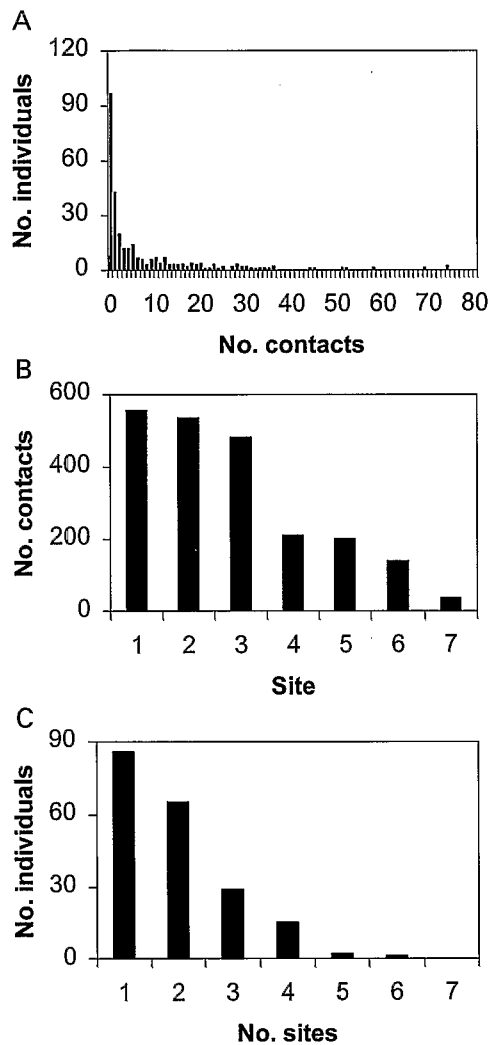


Fig. 6. Field data from Dogofry Ba, Mali. As legend for Fig. 2.

little impact on R_0 unless all major contact sites are included. The impact of focal control depends crucially on the contact pattern; targeting is relatively effective if individuals making most contacts tend to use the same site(s) and is relatively ineffective if these individuals tend to use different sites (Woolhouse *et al.* 1991). Importantly, the impact of focal control measures cannot be accurately predicted unless the contact pattern is known. (The same applies, but to a much lesser degree, to the impact of individual-targeted control measures.)

Clearly, spatial heterogeneity in the distribution of infected snails is important in the context of focal control. Although differences in snail densities between sites only have an impact on overall R_0 if they are correlated with contact rates, they do have an impact on the relative contribution of sites to R_0 . However, this contribution is not linearly related to snail density and it is difficult to offer practical criteria for allowing for this effect, other than that of 2 sites with equal contact rates the one with highest snail densities should be a priority and that a site

should not be a priority just because snail densities are high.

DISCUSSION

The field data show several consistent patterns. Heterogeneities in water contact behaviour have a substantial impact on the basic reproduction number, R_0 , because contacts, and therefore transmission, tend to be concentrated among certain individuals and certain sites. In general, the major contribution to these effects comes from heterogeneity between individuals, with spatial heterogeneities making a lesser, but still significant, contribution. This arises because the distributions of individual contact rates tend to be highly over-dispersed, a pattern which is also seen for vector-borne and sexually-transmitted infections (Woolhouse *et al.* 1997). One important aspect of spatial heterogeneity is the degree to which contacts are shared among different sites; concentrating contacts at one or a few sites can cause very significant increases in R_0 and diffuse patterns of contacts should therefore be encouraged.

The analysis assumes a perfect correlation between exposure and contamination; this correlation has yet to be measured in the field but the analysis should be regarded as giving upper bounds to the impact on R_0 . And the analysis ignores any correlation between contact rates and snail densities across sites; field data have low power to detect any correlation, but the correlation could have significant effects. The analysis also ignores other heterogeneities in the susceptibility or potential infectivity of individuals, although effects due to acquired immunity are not relevant to R_0 . The effect of introducing pre-patent infection of snails into the analysis is simply to scale R_0 by the fraction of snails that survive the prepatent period, which may be low in practice (Woolhouse & Chandiwana, 1989). The effect of introducing schistosomate mating is that $R_0 > 1$ becomes a necessary but not sufficient condition for the establishment of endemic infection (May, 1977).

Effects on relative values of R_0 have been described here, but there are remarkably few good estimates of the absolute value of R_0 for human schistosomes (Anderson & May, 1991). For *S. haematobium* infection at one of the field sites discussed here, Nyamikari in Zimbabwe, one estimate is $R_0 = 4.3$ but this estimate is itself sensitive to consideration of heterogeneities in contact rates and may be as high as 8–9 (Woolhouse *et al.* 1996). However, these moderate values do suggest that appropriately targeted control measures would be highly effective: even if R_0 was as high as 10 at Nyamikari then local eradication would, in principle, be possible by removing just 25% of the population from the transmission cycle.

Table 1. Summary of field data and of impacts of heterogeneous water contact patterns on R_0

(s.d. represents population standard deviation.)

Site	Zimbabwe		Mali		
	Nya	Nah	Man	MC	DB
Total population size	465	850	541	1172	943
Study population size	465	850	337	281	295
Number of contact sites	5	7	9	5	7
Site-days observation	70	294	52	33	33
Total contacts observed	2807	4819	1623	1363	2160
Mean contacts/person	6.04	5.67	4.82	4.85	7.32
s.d. contacts/person	8.57	8.70	6.64	5.73	12.14
Mean contacts/site	561.4	688.4	180.3	272.6	308.6
s.d. contacts/site	148.5	654.6	112.2	107.6	195.1
Mean sites/user	1.63	1.46	2.18	1.79	1.91
s.d. sites/user	0.87	0.71	1.26	0.89	1.02
Individual effect on R_0	3.02	3.35	2.90	2.39	3.75
Site effect	1.07	1.90	1.39	1.16	1.40
Contact pattern effect	1.37	1.02	1.28	1.24	1.23
Overall effect	4.42	6.48	5.15	3.44	6.45
Mean snails/site	10.0	4.7	2.8	3.4	3.7
s.d. snails/site	1.3	2.8	3.2	4.7	3.2
Snail density-contact correlation	+0.09	+0.10	-0.64	+0.30	+0.43

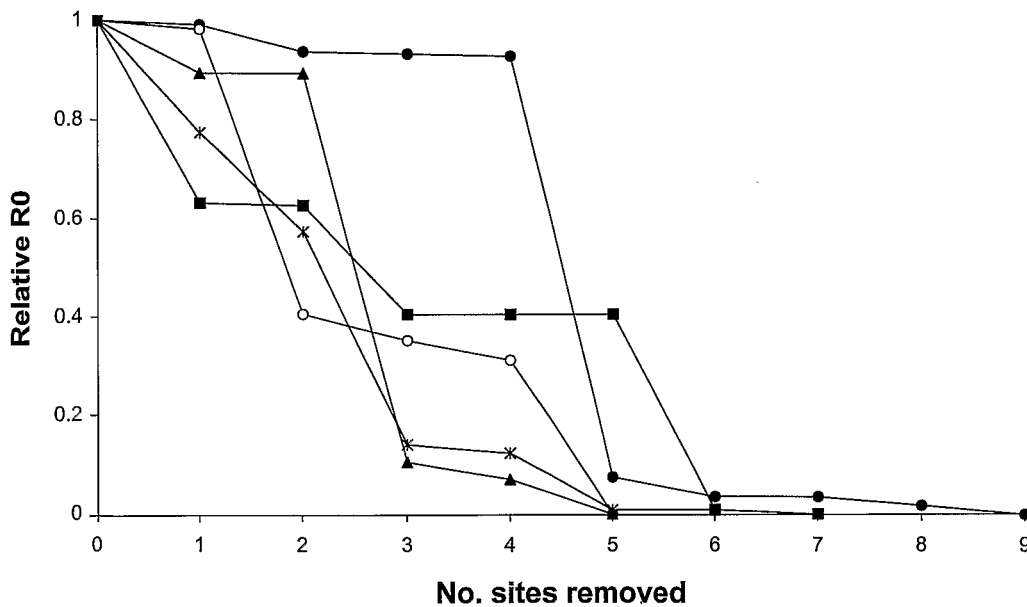


Fig. 7. Effects of focal snail control on the relative value of R_0 . Transmission is prevented at an increasing number of sites in decreasing order of the net contact rate at that site, λ_j . Curves are compared for all 5 field studies (with the number of sites, L , varying between studies): Nyamakari (○); Nagoon (*); Maniale (●); Medina Coura (▲); Dogofry Ba (■).

Practical application of these results requires firstly that individuals contributing most to transmission can be identified. There have been numerous studies showing water contact behaviour to be related to such factors as age, sex, occupation, religion, socio-economic status and proximity to

contact sites (see Woolhouse *et al.* 1991), suggesting that this may be possible. However, a complicating factor is whether individuals' contact rates are consistent through time; no long-term studies of variation in contact rates have been carried out. Identification of contact sites is often straightforward

but the impact of focal control measures cannot be predicted without knowledge of how individuals distribute their contacts among sites, the contact pattern; the field data suggest there is a tendency towards 'selective' use of sites, in which case it is particularly important that all major transmission sites are included in a control programme. Indeed, perhaps the most important conclusion to emerge from this work is that, while heterogeneities in transmission rates imply that targeted control measures may be relatively efficient, they also imply that control will be relatively ineffective if any individuals or sites making a large contribution to transmission are missed by any (targeted or mass) control programme.

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REFERENCES

- ANDERSON, R. M. & MAY, R. M. (1991). *Infectious Diseases of Humans: Dynamics and Control*. Oxford: Oxford Scientific.
- BARBOUR, A. D. (1978). Macdonald's model and the transmission of bilharzia. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **72**, 6-15.
- CHANDIWANA, S. K. & WOOLHOUSE, M. E. J. (1991). Heterogeneities in water contact patterns and the epidemiology of *Schistosoma haematobium*. *Parasitology* **103**, 363-370.
- CHANDIWANA, S. K., WOOLHOUSE, M. E. J. & BRADLEY, M. (1991). Factors affecting the intensity of reinfection with *Schistosoma haematobium* following treatment with praziquantel. *Parasitology* **102**, 73-83.
- DIETZ, K. (1979). Models for vector-borne parasitic diseases. In *Lecture Notes in Biomathematics*, vol. 39 (ed. Barigozzi, C.), pp. 264-277. Berlin: Springer-Verlag.
- DYE, C. & HASIBEDER, G. (1986). Population dynamics of mosquito-borne disease: effects of flies which bite some people more than others. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **80**, 69-77.
- ETARD, J.-F., AUDIBERT, M. & DABO, A. (1995). Age-acquired resistance and predisposition to reinfection with *Schistosoma haematobium* after treatment with praziquantel in Mali. *American Journal of Tropical Medicine and Hygiene* **52**, 549-558.
- ETARD, J.-F. & BOREL, E. (1992). Contacts homme-eau et schistosomiase humaine dans un village mauritanien. *Revue d'Epidemiologie et Sante Publique* **40**, 268-275.
- MAY, R. M. (1977). Togetherness among schistosomes: its effects on the dynamics of infection. *Mathematical Biosciences* **35**, 301-343.
- WOOLHOUSE, M. E. J. (1991). On the application of mathematical models of schistosome transmission dynamics. I. Natural transmission. *Acta Tropica* **49**, 241-270.
- WOOLHOUSE, M. E. J. (1996). Mathematical models of transmission dynamics and control of schistosomiasis. *American Journal of Tropical Medicine and Hygiene* **55**, SS144-SS148.
- WOOLHOUSE, M. E. J. & CHANDIWANA, S. K. (1989). Spatial and temporal heterogeneity in the population dynamics of *Bulinus globosus* and *Biomphalaria pfeifferi* and in the epidemiology of their infection with schistosomes. *Parasitology* **98**, 21-34.
- WOOLHOUSE, M. E. J., DYE, C., ETARD, J.-F., SMITH, T., CHARLWOOD, J. D., GARNETT, G. P., HAGAN, P., HII, J. L. K., NDHLOVU, P. D., QUINNELL, R. J., WATTS, C. U., CHANDIWANA, S. K. & ANDERSON, R. M. (1997). Heterogeneities in the transmission of infectious agents: implications for the design of control programmes. *Proceedings of the National Academy of Sciences, USA* **94**, 338-342.
- WOOLHOUSE, M. E. J., HASIBEDER, G. & CHANDIWANA, S. K. (1996). On estimating the basic reproduction number for *Schistosoma haematobium*. *Tropical Medicine and International Health* **1**, 456-463.
- WOOLHOUSE, M. E. J., WATTS, C. H. & CHANDIWANA, S. K. (1991). Heterogeneities in transmission rates and the epidemiology of schistosome infection. *Proceedings of the Royal Society of London, Series B* **245**, 109-114.