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**EPIDEMIOLOGICAL MODELLING FOR
SCHISTOSOMIASIS CONTROL**

Report of an informal consultation

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Ce rapport exprime les vues collectives d'un groupe international d'experts réuni par le PROGRAMME SPECIAL PNUD/BANQUE MONDIALE/OMS DE RECHERCHE ET DE FORMATION CONCERNANT LES MALADIES TROPICALES (TDR). Il ne représente pas nécessairement les vues du TDR/OMS et, en vue d'une diffusion accélérée, il n'a pas été l'objet d'une mise en forme particulièrement soignée. En outre, les noms géographiques utilisés dans le présent rapport n'impliquent, de la part du TDR ou de l'OMS, aucune prise de position quant au statut juridique de tel ou tel pays, territoire, ville ou zone, ou de ses autorités, ni quant au tracé de ses frontières.

1. INTRODUCTION

Schistosomiasis remains one of the main parasitic diseases affecting the populations of developing countries. Although new tools for the control of the disease have become available over the past decades, their wide-scale implementation remains difficult in many countries due to budgetary and operational constraints. The main challenge is thus to develop structures and strategies to apply and target the available tools in the most cost-effective, feasible and sustainable way. To that end, adequate knowledge and understanding of the epidemiological factors that govern the dynamics of transmission and morbidity, and of the impact of control measures on them, are critical. Major advances have recently been made in understanding the biology and immunology of infection, but basic information on some epidemiological determinants remains incomplete.

Epidemiological modelling can help to identify and bridge these gaps, and to orientate further research. Sufficient information is now available to start modelling the outcome and cost-effectiveness of various control options. The experiences in onchocerciasis control have shown that such approaches can be pragmatically applied and contribute substantially to the planning and evaluation of control interventions.

2. SCHISTOSOMIASIS EPIDEMIOLOGY: STATE OF THE ART

Over the past 90 years, a large body of information has accumulated on the biology, epidemiology and control of schistosomiasis. However, there is much variation in our understanding of the three main species that affect humans (*Schistosoma haematobium*, *S. mansoni* and *S. japonicum*), and there are large gaps in our understanding of particular aspects of infection, morbidity and control.

Although information is emerging concerning exposure of humans to potentially infective water bodies, the relationship between cercarial densities in water and their infectivity to humans is poorly understood. Age specific prevalence and intensity curves have been well described for all three species, and exposure studies provide evidence in support of an age-related resistance to reinfection after chemotherapy of *S. haematobium* and *S. mansoni*. Laboratory studies strongly suggest that a component of this resistance may be immunologically mediated. Estimates of worm longevity exist for all three species, but a major problem, particularly in *S. japonicum*, is the relationship between worm burdens and faecal egg output. Although descriptive information of the contamination of the environment is beginning to emerge for *S. mansoni*, this is not the case for the other two species. In general, the dynamics of the snail intermediate hosts are well described. A major, but insufficiently studied problem in *S. japonicum* is that of non-human reservoir hosts. To a lesser extent primates and rodents may pose a similar problem for *S. mansoni*.

The processes and extent of disease due to schistosomiasis are generally less well understood than the processes of infection. A distinction must be drawn between early and late morbidity, and between direct morbidity on target organs and indirect effects of schistosome infection on growth and development, cognitive function and work capacity. New tools for the assessment of morbidity, such as portable ultrasound machines, are now available, but require standardization in community-based longitudinal studies. These tools should also be valuable in assessing the impact of chemotherapy. A relationship has been demonstrated between current intensity of infection and morbidity in schistosomiasis due to *S. mansoni* and *S. haematobium*, but not to *S. japonicum*. However, the contribution of previous infection, and of other factors including host and parasite genetics, other infections, nutritional status, and maternal infection status, is poorly understood.

The availability of safe and effective drugs for the treatment of all three main species of schistosome has drastically altered approaches to control. The focal application of molluscicides may now be envisioned as an adjunct to community-based chemotherapy, but data are still insufficient to determine the potential role of biological control of snails. There have been a large number of empirical chemotherapy projects but few that have attempted to determine optimal strategies. Quantitative information on the impact of other measures including health education and the provision of water supplies and sanitation is still relatively sparse. There is a need for cost-effectiveness analysis of control programmes and for determining the feasibility of integrating control programmes within existing health care structures.

3. SCHISTOSOMIASIS MODELLING: STATE OF THE ART

Many different models have been developed for schistosomiasis; these take various forms and address a number of different questions. Most relevant here are analytical models of the transmission cycle, models of the relationships between costs and effectiveness, and more detailed and comprehensive simulation models.

The earliest models of schistosome transmission were highly simplified representations of the life-cycle, explicitly considering only mean worm burdens and the prevalence of infection of snails. The models identified that density dependent effects have to be present in the transmission cycle of an endemic disease, and that the parts of the schistosome cycle most likely to show such effects are those in the intermediate and definitive hosts. Macdonald (1965) for example, used the saturation of infection in the snail population as the limiting factor. More recent work suggests that density dependent effects in the definitive host, whether crowding, immune suppression of egg output or protective immunity, probably play an even more important role, and models have been developed to incorporate this. These models are broad in scope, and much detailed modelling of individual components of the transmission cycle has been undertaken, enabling the interpretation and estimation of parameters. Examples of these more specific models

address the infection of snails, the population dynamics of miracidia and cercariae, the relationship between human infection and age in an endemic situation, the consequences of heterogeneities in transmission rates and the impact of acquired immunity. There remains a need to develop further these aspects of the models and to include factors such as reservoir hosts. There is also a need to develop models which consider variables of public health importance, including the dynamics of morbidity, and for models which consider individual species.

There have been a number of studies that have considered the cost-analysis of schistosomiasis control. However, most of these studies have presented composite cost estimates and have not utilized itemized cost menus as would be required for modelling cost-effectiveness. In attempting to relate costs to effectiveness, most studies have tended to use static models expressing effectiveness in terms of drug delivery or cure rate. An alternative approach has been to use a model which incorporates the transmission dynamics of the parasite to permit evaluation of the long-term impact of control. However, these models have only presented effectiveness in terms of reduction in the prevalence of infection or prevention of heavy infection. No model has yet presented effectiveness in terms of morbidity prevention in a form which considers chronicity, concurrent infections, age-dependent variation or the different phases of morbidity.

Computer simulation models are especially useful for planning and evaluation of control strategies. They can take account of the specific characteristics of the population dynamics and epidemiology, including e.g., risk strata. Control options can be specified, including coverage and compliance patterns, and disease dynamics can be predicted under different control options. Comprehensive simulation models can profit greatly from the achievements of analytical models for describing parts of the transmission cycle and from specific studies of natural history, morbidity and costs. In the micro-simulation approach, individual life-histories are generated according to the model assumptions, and later on aggregated towards populations. Model output can be presented in a form similar to that used in the analysis of field research data, and this enables a detailed comparison between predicted and observed epidemiological results. The microsimulation approach is highly flexible and has recently proven to be useful in planning and evaluation of onchocerciasis control.

4. THE VALUE OF MODELS

The biological complexity of the schistosome life cycle makes it difficult to develop a quantitative understanding of schistosome epidemiology and to select from the wide range of available control options. However, extensive data are available from previous and current research which make schistosomiasis a suitable subject for development of epidemiological models. These models have the potential to improve our understanding of the epidemiology of schistosomiasis and our assessment of the expected impact of control

programmes. Models can also assist in extrapolation of the results from field trials, which usually are of relatively short duration, to alternative designs for control on the long term. The development of models is dependent on close interactions between mathematicians, biologists, physicians, social scientists and health planners, both to decide on the questions model development should address, and to determine the epidemiological and operational variables and processes, which should be included in the models to answer the questions posed.

It is essential that the model structure reflects a good understanding of schistosome biology and that parameter estimates are based on suitable field data. The assumptions of the models must be clearly stated, and model output should be validated against field data.

The following areas are identified as especially important for further model development and application:

- the assessment of the potential impact of specific control programmes on morbidity and public health;
- comparative costs and impacts on infection, transmission and morbidity of different chemotherapy strategies (e.g., selective vs mass chemotherapy, different treatment intervals);
- the additional impact and cost-effectiveness of snail control, water supply and health education;
- comparative efficiency of specific schistosomiasis control vs Primary Health Care programmes vs integrated multi-disease control programmes;
- evaluation of possible future scenarios, e.g., interventions based on vaccines or on biological control, or the development of drug resistance;
- prediction of the usefulness of rapid assessment methods for individual screening and for identification of high risk communities;
- identification of research questions and research priorities.

5. NEEDS FOR FIELD RESEARCH

Extensive studies have already been undertaken and much existing data remains to be analyzed in more detail. In addition, the following topics were identified as areas of special relevance to the development of epidemiological models for schistosomiasis control which require further field research. It should be emphasized that longitudinal studies are of special importance.

5.1. Disease process

- measures of morbidity and standardization of data collection;
- relationships between morbidity measures, infection intensity, history of infection, and age;
- variation in susceptibility to morbidity due to other infections, host genetics, parasite genetics, maternal infection status and nutritional status;
- the impact of (repeated) chemotherapy on morbidity;
- the impact of history of infection and of treatment on the subsequent development of morbidity.

5.2. Public health importance

- impact of infection on such factors as growth and development, work capacity, cognitive development and school attendance and performance;
- measures of the perceived importance of schistosomiasis to the individual, such as health-seeking behaviour and personal expenditure, and compliance with available control programmes.

5.3. Transmission cycle

- standardization of exposure and contamination indices;
- the roles of exposure, acquired immunity and physiological factors in determining rates of infection and reinfection;
- the effects of (repeated) chemotherapy on acquired immunity;
- the effects on human infection of heterogeneities in snail densities and snail infection;
- the relationships of stool and urine egg counts and other indices of infection (e.g., circulating antigens) with worm burden;
- the role of animal reservoirs.

5.4. Control

- identification of communities at high risk of disease;
- impacts of different chemotherapy programmes;
- operational performance, such as coverage, compliance, diagnostic sensitivity and itemized cost data;

- geographic variability in the effectiveness of control programmes;
- impact of different molluscicides (synthetic or plant material) and biological control;
- impact of improved sanitation, water supply and health education programmes.

6. CONCLUSION

Epidemiological modelling has the potential to become an equally important, practical tool for the planning and evaluation of schistosomiasis research and control, just as it has become for another helminth disease, onchocerciasis. Further development and application of epidemiological modelling of schistosomiasis, therefore, is strongly encouraged. However, it is essential that this involves a dynamic collaboration between modelers and field researchers. The importance of such collaboration cannot be overemphasized and the fruitful interaction between modelers and epidemiologists during the present meeting provided a very positive example in this respect. Maximum impact of models will require the use of these tools by research planners, major funding agencies as well as the managers of control programmes, and this should be taken into account in model development and application.

7. Selected references on epidemiological modelling of helminth diseases

A few selected references on epidemiological modelling of helminth diseases, which are of direct relevance to the issues discussed in this report, are given below. Furthermore, it is intended that the working papers for the meeting are published in a supplement to the American Journal of Tropical Medicine and Hygiene in 1993.

Anderson R.M. and Medley G.F. (1985). Community control of helminth infections of man by mass and selective chemotherapy. *Parasitology* 90, pp 629-660.

Guyatt H.L., Bundy D.A.P. and Evans D. (1992). A population dynamic approach to the cost-effectiveness analysis of community-based anti-helminthic treatment: effects of treatment frequency. House economic research working paper no.1 (n/d). Swiss Tropical Institute, Basel.

Habbema, J.D.F., Plaisier A.P., Alley E.S. and Remme J. (1991). Epidemiological modelling for onchocerciasis control. *Parasitology Today* 8, pp 99-103.

Macdonald G. (1965). The dynamics of helminth infections, with special reference to schistosomes. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 59, pp 489-506.

May R.M. (1977). Togetherness among the schistosomes: its effects on the dynamics of infection. *Mathematical Biosciences* 35, pp 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. (1991). On the application of mathematical models of schistosome transmission dynamics. II. Control. Acta Tropica 50, 189-204.

Figure 1: Schematic representation of the transmission cycle, monitoring indicators and available options for control of schistosomiasis.

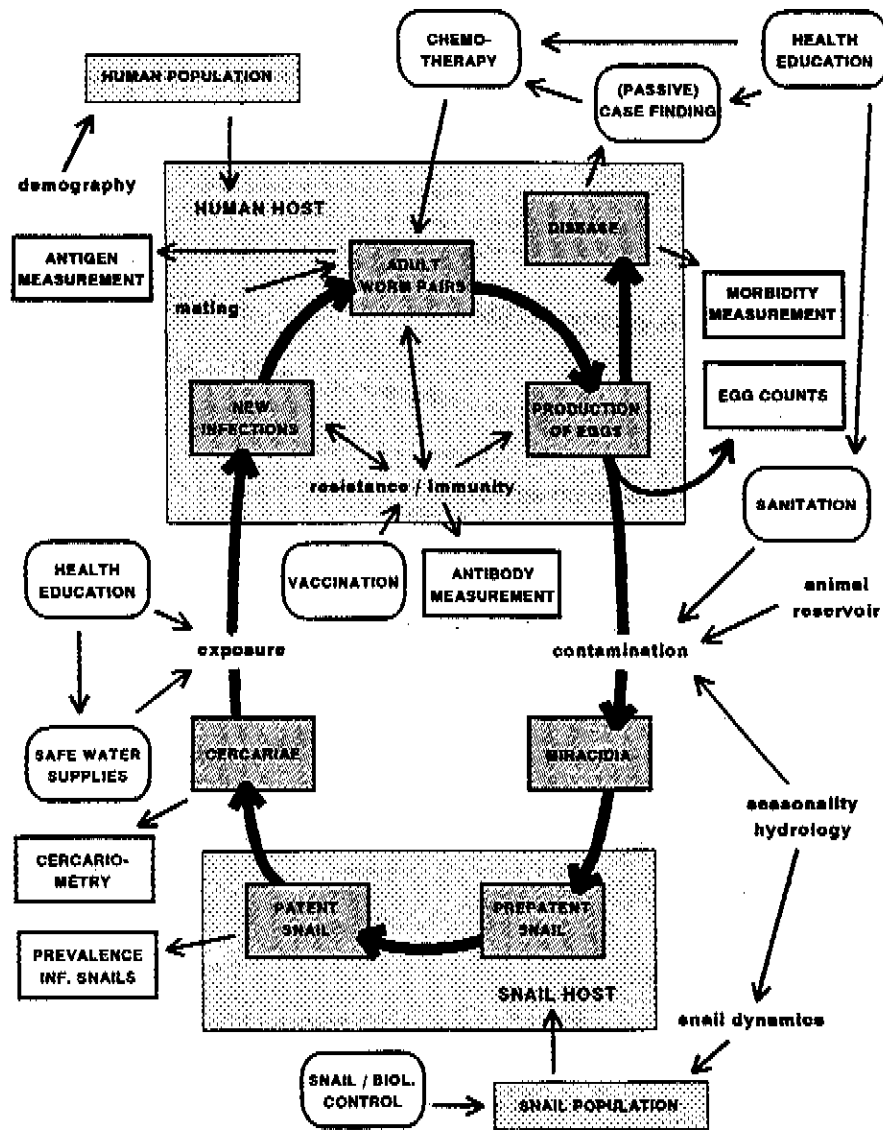


Table 1: The current status of knowledge on processes or parameters that are relevant for modelling the three main schistosomiasis species, ranging from fair amount of information available (++) , little information available (+) to virtually no information available (-). Behind the headings the state of the art in modelling is indicated (with same ranges).

MODELLING PARAMETER OR PROCESS	<i>S. haem</i>	<i>S. man</i>	<i>S. jap</i>
Acquiring new infections (+)			
New infections per cercaria	-	-	-
Heterogeneity and age/sex differences in exposure	++	++	-
Resistance innate or acquired	+	+	-
Role of infection history in immune status	+	+	-
Demography (+ migration)	+	+	-
Dynamics of established infections (-)			
Mating probability	-	-	-
Lifespan of worms	+	++	+
Pattern of egg production (eg. prepatent period)	+	+	+
Density dependence in egg production	-	+	-
Delay in egg excretion after production	-	+	-
Retention of eggs in tissues	-	+	+
Effect of immunity on (fecundity of) adult worms	-	-	-
Dynamics of human to vector transmission (+)			
Heterogeneity and age/sex differences in contamination	+	+	-
Dynamics of contamination	-	-	-
Relationship between contamination and exposure	-	-	-
Proportion of eggs that hatch after reaching water	-	+	-
Miracidial population dynamics	-	+	-
Snails infected per miracidium	+	+	+
Importance of animal reservoir	+	+	++
Dynamics of infection in vector (++)			
Snail dynamics	++	++	++
Spatial/temporal distribution of snails	+	++	++
Effect of infection on snail mortality and fecundity	++	++	+
Cercaria production	++	++	+
Duration and pattern of shedding	++	++	+
Cercarial population dynamics	+	+	+

Morbidity/disease (-)

Relation infection to early morbidity
 Relation infection to late morbidity
 Indirect morbidity (eg. reduced growth, development)
 Reversibility of pathology
 Role of immuno-genetic susceptibility
 Interaction with concomitant infections
 Parasite related factors (eg. strains)
 Mortality
 Costs of disease

+	+	+
+	+	+
-	-	+
+	+	-
-	-	+
-	-	-
-	-	+
+	+	+
+	+	+

Monitoring and control (+)

Monitoring (indicators)

Relation infection and egg counts
 Relation infection and other measurements (eg. serology)
 Snail infection rates, cercariometry
 Incidence and reinfection rates
 Costs of monitoring

+	+	-
+	+	+
+	+	-
+	+	+
+	+	-

Chemotherapy

Coverage
 Rates and patterns of compliance
 Rates and patterns of cure
 Costs of drugs
 Costs of drug distribution

+	+	+
+	+	+
+	+	++
++	++	++
+	+	+

Other control strategies

Area coverage of snail/biological control
 Proportion of snails killed after snail/biological control
 Impact of sanitation
 Impact of providing safe water supplies
 Passive case finding (eg. state of disease to seek care)
 Impact of health education (on compliance, sanitation, etc.)
 Impact of vaccination
 Costs of control

+	+	+
++	++	++
+	+	-
-	+	-
+	+	-
-	-	-
-	-	-
+	+	+

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